

23-2553

IN THE
United States Court of Appeals
FOR THE THIRD CIRCUIT

UNITED STATES OF AMERICA EX REL.,
STEPHEN A. KRAHLING; JOAN A. WLOCHOWSKI,

against

MERCK & CO, INC.,

STEPHEN A. KRAHLING; JOAN A. WLOCHOWSKI,

Appellants.

*On Appeal from the United States District Court
for the Eastern District of Pennsylvania
The Honorable Chad F. Kenney, Case No. 2:10-04374-CFK*

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(Filed Under Seal)**

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1 A. I'm being represented by
 2 Mr. Chris Hall from Saul Ewing and Lisa
 3 Dykstra from Morgan Lewis.
 4 Q. Have you ever been deposed
 5 before?
 6 A. Yes, I have.
 7 Q. In what kind of case?
 8 A. One was a -- many, many years
 9 ago, a Securities and Exchange Commission case
 10 that -- typical Securities and Exchange
 11 Commission case. It was, in general, in terms
 12 of who said what to whom in various
 13 circumstances. And then there was a
 14 subsequent case that was very similar to that
 15 basically.
 16 Q. Also involving securities?
 17 A. Generally involving securities.
 18 Q. Were you ever deposed in a case
 19 involving any medical or pharmaceutical
 20 issues?
 21 A. No, not at all. The ones
 22 involving securities was simply because I was
 23 aware of transactions that were ongoing.
 24 Q. Was Merck a party to those
 25 cases?

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1 A. The first one, yes.
 2 Q. About what year was that case?
 3 A. That was 1980s, early 1990s.
 4 Q. Have you met with your -- with
 5 your counsel prior to --
 6 A. Just to correct, Merck was not a
 7 party to it, the parties that were involved
 8 was the Security and Exchange Commission and a
 9 private citizen, but it related to a
 10 transaction that Merck was a party to just
 11 while I was there.
 12 Q. And have you met with your
 13 attorneys prior to the deposition?
 14 A. At this deposition, yes. Yes, I
 15 have.
 16 Q. When?
 17 A. We've had several meetings, the
 18 most recent one being yesterday; and then two
 19 prior to that, which were several months ago,
 20 I believe.
 21 Q. Which lawyers did you meet with?
 22 A. Lisa Dykstra was there and Chris
 23 Hall were present.
 24 Q. Anyone else?
 25 A. There were -- I believe you were

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1 in the room, weren't you? Yes. Yes, you
 2 were. Sorry if I don't remember entirely.
 3 Q. You being?
 4 A. I'm sorry.
 5 Q. Lindsey?
 6 A. Lindsey. Lindsey Mills. I'm
 7 sorry.
 8 Q. Okay.
 9 MR. HALL: Lindsey Mills.
 10 THE WITNESS: Lindsey Mills was
 11 definitely present, yesterday. I just
 12 couldn't remember previously. I'm
 13 sorry.
 14 BY MR. BEGLEITER:
 15 Q. Have you ever testified at a
 16 trial?
 17 A. No, I have not.
 18 Q. Did you review documents prior
 19 to this deposition?
 20 A. Yes.
 21 Q. And did any of these documents
 22 refresh your recollection?
 23 A. The documents generally refreshed
 24 my recollection of things that were happening.
 25 They did not necessarily reflect my -- refresh

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1 my recollection of actual events that
 2 occurred.
 3 Q. I'm trying to understand --
 4 A. I saw -- well, the refreshing of
 5 the recollection -- that's a fair question.
 6 The refreshing of the recollection was that
 7 when I saw the documents, I certainly
 8 recollected the events that occurred. But if
 9 the question was do I actually remember the
 10 occurrence of the events? With the exception
 11 of a couple of occasions, the answer is no,
 12 because it was, after all, close to 20 years
 13 ago.
 14 Q. Can you tell me which documents
 15 refreshed your recollection?
 16 A. I told you --
 17 MS. DYKSTRA: Objection. The
 18 documents we prepared for Mr. --
 19 Dr. Emini are protected by privilege.
 20 I don't know if there is a specific one
 21 that he recalls, but if there is a
 22 specific document that he recalls that
 23 refreshes his recollection, I'll let
 24 him identify it for you.
 25 MR. BEGLEITER: Okay. Great.

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1 BY MR. BEGLEITER:
 2 Q. Is there any specific document
 3 that you recall?
 4 A. It was the entire ream of
 5 documents we were looking at.
 6 Q. What's your position with the
 7 Bill & Melinda Gates Foundation?
 8 A. I am the Director of the Global
 9 HIV Program with the foundation.
 10 MS. DYKSTRA: Dr. Emini, I think
 11 the court reporter is going to ask you
 12 to slow down just a little bit.
 13 THE WITNESS: Oh, I shall. I
 14 shall.
 15 BY MR. BEGLEITER:
 16 Q. How long have you been at the
 17 Bill & Melinda Gates Foundation?
 18 A. This July will be two years.
 19 Q. And would it be correct to say
 20 that you're focusing on AIDS research?
 21 A. Yes, it is.
 22 Q. Anything more than just research?
 23 A. Well, it is research, the Bill &
 24 Melinda Gates Foundation funds research
 25 efforts. It also funds what we call delivery

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1 efforts which is how to get the fruits of
 2 those research to individuals at risk of HIV
 3 or suffering from HIV infection in specific
 4 parts of the world that are of focus for the
 5 foundation. In the case of HIV, that would be
 6 Southern and Eastern Africa.
 7 Q. Can you tell me -- you did work
 8 for Merck?
 9 A. Yes, I did.
 10 Q. Can you tell me approximately
 11 when you started and when you ended?
 12 A. I started in August of 1983 and
 13 left at the end of January 2004.
 14 Q. And what were the circumstances
 15 of your leaving?
 16 A. It had been 22 years that I was
 17 at the company, and I decided that 22 years
 18 was long enough. At the time the company had
 19 a program in place to permit early retirement
 20 with full benefits associated with early
 21 retirement, and I raised my hand. And since
 22 it had been that period of time, I took the
 23 opportunity.
 24 Q. So your departure was amicable?
 25 A. Totally amicable.

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1 Q. Did your departure have anything
 2 to do with, we haven't defined yet, but I
 3 think you'll know, Protocol 007?
 4 A. No, not at all.
 5 Q. Did it have anything to do with
 6 the MMR II vaccine?
 7 A. Not at all.
 8 Q. I want you to take a look at
 9 Emini-1.
 10 - - -
 11 (Exhibit Emini-1, Curriculum
 12 vitae, was marked for identification.)
 13 - - -
 14 BY MR. BEGLEITER:
 15 Q. I'd like to show you -- I'd like
 16 to hand the court reporter and you and your
 17 counsel a document. I don't know how it was
 18 marked, but it's marked 00001 EMINI. We'll
 19 call this Emini-1 for this deposition. Just
 20 what is this, sir?
 21 A. This is my curriculum vitae as
 22 of January 2016.
 23 Q. Did you prepare this curriculum
 24 vitae?
 25 A. Yes, I did.

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1 Q. As far as you know, is it
 2 accurate?
 3 A. As far as I'm aware, yes.
 4 Q. Up to January 2016?
 5 A. Yeah, it is.
 6 Q. Is it?
 7 A. Yes. It does appear to be the
 8 one that I prepared up until that time, yes.
 9 Q. And tell me, sir, have there
 10 been any changes since January 2016 that you
 11 would ordinarily put in your curriculum vitae?
 12 A. There may very well have been.
 13 There are probably one or two additional
 14 publications that were published since then
 15 that would have wound up on the publication
 16 list. And I was recently elected a Fellow of
 17 the College of Physicians of Philadelphia, and
 18 that would have been included.
 19 Q. Congratulations on that.
 20 If we can go back, if you can go
 21 to the "PROFESSIONAL HISTORY" section, which
 22 begins towards -- about two-thirds of the way
 23 down the first page and ends about a third of
 24 the way down the second.
 25 A. Yes.

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<p style="text-align: right;">Page 18</p> <p>1 Q. And just a few questions about 2 your professional history. 3 A. Yes, please. 4 Q. Looking at Item 10, Director of 5 HIV Biology and Immunology at Merck Research 6 Laboratories, do you see that? 7 A. Yes, sir. 8 Q. Did you have any responsibility 9 for clinical trials as a Director of HIV 10 Biology and Immunology? 11 A. My direct responsibility was in 12 supportive research. 13 Q. I see. 14 A. In supportive research. But the 15 clinical, the medical group did not report to 16 me at Merck. It was the research group. 17 Q. When did -- and the research 18 group would not have included clinical 19 research? 20 A. The research group would not 21 normally have included clinical research, no. 22 Q. Can you tell me which one of 23 these numbers was the first time that you 24 began to have any involvement with clinical 25 research?</p>	<p style="text-align: right;">Page 20</p> <p>1 research group? 2 A. No. It was an independent group. 3 Q. You were -- let's go to number 4 8. Executive Director of Department of 5 Antiviral Research. What were your duties as 6 the Executive Director of Department of 7 Antiviral Research? 8 A. The same thing. I was 9 responsible for the research efforts that led 10 to the development of antiviral drugs. 11 Q. Did that include mumps research? 12 A. No, these were antiviral drugs. 13 These are chemotherapeutics. These are not 14 vaccines. 15 Q. Did the Department of Antiviral 16 Research exist before you became the executive 17 director? 18 A. No, I was actually the founding 19 executive director of the Department of 20 Antiviral Research. 21 Q. Let's go to number -- you were 22 the executive director -- number 7 is you're 23 Vice President of Vaccine and Biologics 24 Research? 25 A. Yes, that's right.</p>
<p style="text-align: right;">Page 19</p> <p>1 A. Involvement with clinical 2 research was, I guess the word I would use is 3 ancillary in the sense that the nature of how 4 we operated within the organization was an 5 open operational collaboration between 6 regulatory and medical research and the 7 research laboratories, where I was in research 8 group which -- that I was responsible for. So 9 there would be occasions where in the 10 preparation of regulatory documents or in the 11 conduct of research, they would be in 12 support -- in the conduct of activities that 13 would be in support of clinical activities 14 that would have occurred. 15 Q. Did you -- was there a time in 16 which you had a supervisory role with regard 17 to clinical research? 18 A. Not in the context of a 19 clinical -- not in the context of the 20 execution of the clinical research, per se. 21 In other words, the execution of the clinical 22 protocol. That would have been the 23 responsibility of the medical research group. 24 Q. And did you have any supervisory 25 responsibility with regard to the medical</p>	<p style="text-align: right;">Page 21</p> <p>1 Q. Was 8 to 7 a promotion? 2 A. From 7 to 8. So when I -- 3 Q. 7 to 8. 8 would be -- just to 4 be clear, 8 is further back in time, 7 is more 5 recent. 6 A. Yes, I'm sorry, reading 7 backwards. Yes. So, yes, it was. I mean, 8 vice president is a higher level than an 9 executive director. 10 So after I completed what was 11 approximately five years as the head of the 12 Department of Antiviral Research, the efforts 13 we were originally formed to do had, in fact, 14 largely been completed and then the position 15 became available at the head of vaccines 16 research. I was offered the position. And I 17 took it. 18 Q. And as number 8 did you have any 19 responsibility, supervisory responsibility for 20 any clinical research? 21 A. It was the same setup. The 22 medical research group, there's always a 23 separate operation, a separate reporting 24 relationship than the research group. 25 Q. I just need a clarification.</p>

6 (Pages 18 - 21)

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1 You know a Dr. David Krah?
 2 A. Yes.
 3 Q. Were you his -- was there a time
 4 in which you were a supervisor of Dr. Krah?
 5 A. I was -- he was in my
 6 department, so I was the supervisor of his
 7 supervisor.
 8 Q. And as a -- and what did you
 9 supervise him doing?
 10 MS. DYKSTRA: Objection.
 11 BY MR. BEGLEITER:
 12 Q. What was he doing that you
 13 supervised him for?
 14 MS. DYKSTRA: Objection.
 15 BY MR. BEGLEITER:
 16 Q. Go ahead.
 17 MS. DYKSTRA: Form.
 18 BY MR. BEGLEITER:
 19 Q. Okay. What was his job when you
 20 were supervising him? Ask it that way.
 21 A. His job was to run a research
 22 laboratory. That was his -- that was his
 23 predominant job, just like everybody else in
 24 the group.
 25 Q. And was this -- was he -- he was

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1 doing research into the blood of children who
 2 either had mumps or had received mumps MMR II?
 3 A. You're referring to a different
 4 set of circumstances. So as I said earlier,
 5 even though the medical research group was
 6 separate from us, we were a large
 7 collaborative operation. So there would be
 8 occasions, and this was true for regulatory
 9 and medical and research, where there would be
 10 activities that would be conducted by one
 11 group, okay, but would essentially be in
 12 support of another group.
 13 Q. What group was Dr. Krah in?
 14 A. So Dr. Krah was formally in this
 15 group, which is my group, which is the
 16 research group.
 17 Q. And what was his job?
 18 A. His job, his job was to conduct
 19 whatever research needed to be conducted plus
 20 whatever other activities needed to be done in
 21 support of the goals of the research group and
 22 in support of collaborative work that we did
 23 with the other groups such as medical and
 24 regulatory. But that was all of our jobs.
 25 Q. The -- when it came to staffing,

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1 did you have any responsibility in staffing
 2 decisions in Mr -- in Dr. Krah's laboratory?
 3 MS. DYKSTRA: Objection to form.
 4 I'm not sure what time frame you're
 5 talking about.
 6 MR. BEGLEITER: I'm talking
 7 about the time frame of number 8. I
 8 should have said that.
 9 THE WITNESS: I did not --
 10 MS. DYKSTRA: I'm sorry, number
 11 8 is antiviral research.
 12 BY MR. BEGLEITER:
 13 Q. Number 9 -- number 7, excuse me.
 14 Number 7.
 15 MS. DYKSTRA: Thank you.
 16 THE WITNESS: I delegated
 17 staffing responsibilities to the senior
 18 staff in the department.
 19 BY MR. BEGLEITER:
 20 Q. Who is that? Was there a
 21 particular person who had that responsibility
 22 for Dr. Krah?
 23 A. That would have been his direct
 24 supervisor which would have been Dr. Alan
 25 Shaw, who would have worked in collaboration

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1 with Dr. Krah at the laboratory.
 2 Q. All right. Was this
 3 relationship the same from April '97 to
 4 January '02 as number 7 indicates you held
 5 that position?
 6 A. That would have generally been
 7 true, yes. Though I can't attest to the exact
 8 timing, but Dr. Shaw did report to me up until
 9 such time as I left the company.
 10 Q. Now, Dr. Krah's group was doing
 11 clinical trial. Is that right?
 12 A. No, he was not performing a
 13 clinical trial.
 14 Q. Was he working in support of a
 15 clinical trial?
 16 A. He did work in support of a
 17 specific clinical trial, yes.
 18 Q. Tell me what specific clinical
 19 trial.
 20 A. The one trial that we just
 21 mentioned which was the 007 mumps trial.
 22 Q. What's the purpose of clinical
 23 trials?
 24 A. The purpose of clinical trials
 25 is to generate data in a clinical setting and,

7 (Pages 22 - 25)

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<p style="text-align: right;">Page 26</p> <p>1 therefore, in humans to answer a specific 2 question. 3 Q. Is the purpose to determine -- 4 is the purpose to develop a vaccine? Is the 5 purpose when it comes to the kind of thing 6 that Dr. Kraus was doing to test the vaccine? 7 What was the purpose specifically? 8 A. It could have been, it could 9 have been, it could have been anything. The 10 specific purpose of the clinical study is 11 defined in the specific goals of the clinical 12 trial as defined by the protocol of the study. 13 Q. Was one of the purposes of the 14 clinical trial that Dr. Kraus was involved with 15 to assess efficacy of the MMR II vaccine? 16 A. I do not recall the exact 17 wording of the specific trial goals as defined 18 in the protocols, but it was not to -- it was 19 not to assess efficacy because the vaccine's 20 effectiveness and efficacy had been defined 21 many years previously in a former trial for 22 efficacy. 23 Q. Was it to study the immunogenicity 24 of the vaccine? 25 A. It was designed to, best of my</p>	<p style="text-align: right;">Page 28</p> <p>1 second, but that question certainly 2 involved 007. 3 THE WITNESS: 007, yes. 4 BY MR. BEGLEITER: 5 Q. It was important that the MMR II 6 be safe and effective. Right? 7 MS. DYKSTRA: Objection. 8 THE WITNESS: Well, it was 9 important that the MMR II, as is true 10 for any vaccine, be safe and effective, 11 yes, of course. Or for that matter, 12 any pharmaceutical product. 13 BY MR. BEGLEITER: 14 Q. Now, before a clinical trial 15 began at -- withdrawn. 16 Was Protocol 007, had it begun 17 by the time you arrived -- you became number 18 7? 19 A. I do not recollect. 20 Q. Have you heard of Protocol 006? 21 A. I have no recollection of 006. 22 Q. Do you recall that there was a 23 head-to-head trial of Priorix and MMR II? 24 A. I do recall that there was such 25 a trial, yes.</p>
<p style="text-align: right;">Page 27</p> <p>1 recollection, to study the immunogenicity of 2 the vaccine using a specific set of assays as 3 a measure of that immunogenicity, yes. 4 Q. And the assays, if you recall, 5 were what? 6 A. There were two specific assays. 7 One was an assay referred to as a plaque 8 reduction neutralization assay. And the other 9 one was an assay that was referred to as an 10 ELISA assay, both developed to measure 11 antibody responses elicited by the vaccine. 12 Q. Was it designed to study safety? 13 MS. DYKSTRA: Objection. 14 BY MR. BEGLEITER: 15 Q. Was it designed to study safety? 16 You can answer. 17 A. It was -- again, it depends on 18 what was written and I don't -- I did not 19 review the protocol so I don't know what was 20 written as a specific objective of the study. 21 MS. DYKSTRA: Just to be clear, 22 when we're saying it and the study, 23 you're talking about 007? 24 MR. BEGLEITER: Yes, 007. I'm 25 actually going to switch gears in a</p>	<p style="text-align: right;">Page 29</p> <p>1 Q. Was that trial, to your 2 recollection, in progress when you became 3 number 7, Vice President of Vaccine and 4 Biologics Research? 5 A. I do not know. I don't recollect. 6 Q. Now, in 006, did you make any 7 scientific -- excuse me, withdrawn. You don't 8 know what 006 is. 9 In the study that's done the 10 head-to-head comparison of Priorix and MMR II, 11 did you make any scientific decisions? 12 A. Not to my recollection. 13 Q. Did you make any clinical 14 decisions with regard to that? 15 A. Not to my recollection. 16 Q. How about research decisions? 17 A. Not to my recollection. 18 Q. Were you on any committees while 19 you were at Merck? 20 A. I was on several committees, 21 yes. 22 Q. Can you tell me what committees 23 you were on, let's say, from 1997 on? 24 A. I can't give you the specific 25 details because I don't even remember what</p>

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1 they were called, to be honest with you,
 2 because this is well over 20 years ago. Well,
 3 close to 20 years ago. So but I do recall
 4 certainly being on a research management
 5 committee, I believe it's still referred to
 6 that way, which was a -- literally what it
 7 entails is a research management committee.
 8 I may have served as not
 9 necessarily a committee member but as an
 10 observer to other committees such as
 11 committees related to clinical study design
 12 and things of that nature. Chances are I
 13 would have been an observer and an expert, if
 14 you will, present, but not making any
 15 decisions. As a matter of fact, now that I
 16 recall back, I was not a formal member of that
 17 committee. I remember making presentations to
 18 the committee, but I was never a formal member
 19 of the committee.
 20 Q. Were you involved in any
 21 committees -- committee, I'll give you the
 22 name and tell me if you -- it jogs your
 23 recollection, the Critical Assay Subcommittee,
 24 CAS?
 25 A. I remember the committee, but I

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1 do not believe I was a member.
 2 Q. Were you involved in something
 3 called the Vaccine Assay Committee?
 4 A. I do not recollect, but I don't
 5 believe I was a member.
 6 Q. Did you -- were you a member of
 7 the Vaccine Marketing Committee?
 8 A. I don't even recall that
 9 committee, but I doubt I would have been a
 10 member because normally someone from research
 11 would not have been part of the marketing
 12 committee.
 13 Q. How about the Vaccine Product
 14 Approval Committee, were you a member of that?
 15 A. Again, that is probably a
 16 marketing and regulatory committee. I don't
 17 recall the committee directly, but, again, I
 18 doubt I would have been a formal part of it.
 19 Q. Did you ever attend any meetings
 20 of committees regarding competition?
 21 A. I do not recollect any
 22 specifically.
 23 Q. Let me go back now to Protocol
 24 007. I asked you questions about Protocol
 25 006.

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1 Were you involved -- did you
 2 make scientific decisions regarding the
 3 conduct of Protocol 007?
 4 A. I don't recollect directly, but
 5 I don't believe I did.
 6 Q. How about any clinical decisions
 7 regarding the conduct of 007?
 8 A. No, I did not because I would
 9 not have been permitted to do that.
 10 Q. Can you explain why you weren't
 11 permitted?
 12 A. Again, clinical decisions were
 13 the responsibility of the medical clinical
 14 group. That was not my group and I was not
 15 responsible for that group.
 16 Q. Do you recall the years '97 to
 17 2002 which is number 7 on your list, who was
 18 in charge of that group?
 19 A. I do not recall.
 20 Q. Did you make any research
 21 decisions regarding Protocol 007?
 22 A. I made -- I don't recall any
 23 specific decisions related to the protocol.
 24 There were activities that went on related to
 25 the protocol in which I was involved and

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1 participated.
 2 Q. Did you -- were you consulted by
 3 others in the conduct of 007?
 4 MS. DYKSTRA: Objection. Form.
 5 THE WITNESS: I was consulted
 6 with regards to the assays that were
 7 developed and run in support of the
 8 study.
 9 BY MR. BEGLEITER:
 10 Q. What assets of the assays were
 11 you consulted on?
 12 A. Well, the assays were being
 13 conducted in the laboratory of Dr. David Krahn,
 14 and there were some questions that arose with
 15 regard to the assays. And because it was in
 16 my employment relationship, I was obviously
 17 consulted.
 18 Q. Do you recall any of what those
 19 questions were?
 20 A. The questions that arose, the
 21 ones that I recollect very clearly are the
 22 questions that arose subsequent to an FDA
 23 inspection that occurred of the laboratory in
 24 which the FDA inspector noted, if I recall,
 25 four very specific observations that were part

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<p style="text-align: right;">Page 34</p> <p>1 of a formal report from the agency and from 2 the inspector known as a Form 483. I recall 3 that correctly because that Form 483 was 4 because of my level, handed directly to me by 5 the inspector. 6 Q. Was it appropriate for the 7 inspector to hand it to you considering your 8 responsibilities or should it have been handed 9 to somebody else? 10 A. No, because the inspection was 11 related specifically to Dr. David KraH's 12 laboratory and what was going on in there; and 13 because I was, as noted, the most senior level 14 person in that reporting relationship, I was 15 the person. 16 Q. So when you said no -- you began 17 your answer with no, and people do that all 18 the time, so does that really mean yes, you 19 were the right person? 20 A. Yes, I was the right person. 21 The answer to your question, no, I was not the 22 wrong person. 23 Q. So tell me, so there was this 24 reporting relationship between you and 25 Dr. KraH?</p>	<p style="text-align: right;">Page 36</p> <p>1 Ford-Hutchinson's title, if you recollect? 2 A. I honestly don't recollect. I 3 mean, it was obviously a more senior title 4 than mine, but I can't tell you. 5 Q. How did his responsibilities 6 differ from yours? 7 A. He had broader responsibilities 8 over an entire range of departments within the 9 research laboratories, all research 10 departments. Again, clinical was a separate 11 sphere of activities. So was regulatory. 12 Q. And the vaccine and biologics 13 research in '97 to 2002 was just involved with 14 clinical research, is that right, clinical 15 studies? 16 A. No. Again, that was my 17 department. That was the one that was 18 involved with research. 19 Q. I see. But that was your 20 responsibility? 21 A. Research. 22 Q. Research. Okay. 23 A. Just as it says. Vaccine and 24 Biologics Research. 25 Q. Clinical research?</p>
<p style="text-align: right;">Page 35</p> <p>1 A. Well, Dr. KraH, again, was in my 2 department, his direct reporting relationship 3 was with Dr. Shaw who was my direct report. 4 Q. And who did you report to in 5 those years, number 7? 6 A. I believe, and, again, this is 7 because I reported to a fairly large number of 8 individuals over time because of the 22 years 9 I spent in the company, but upon review of the 10 documents, it appeared that at that time my 11 direct supervisor was Dr. Anthony Ford-Hutchinson. 12 Q. Can you repeat the last name, 13 please? 14 A. Ford-Hutchinson. 15 Q. Who did Dr. Anthony Ford-Hutchinson 16 report to? 17 A. He reported to at the time, if I 18 recall correctly, was directly to Dr. Edward 19 Scolnick who was the head of the research 20 laboratories. Though by that time, Dr. Peter 21 Kim had joined the company. I don't recall 22 exactly the time when that happened. So there 23 was some reporting relationship changes that 24 occurred as a result of that at the time. 25 Q. And what was Dr. Anthony</p>	<p style="text-align: right;">Page 37</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: No, clinical 3 research was a function of the clinical 4 research group. There were 5 collaborative events between my 6 department, vaccine and biologics 7 research, and the vaccine clinical 8 research group. But the responsibility 9 was the clinical research group for the 10 conduct of clinical studies. 11 BY MR. BEGLEITER: 12 Q. Were you ever asked to consult 13 on compliance defense for MMR II? 14 MS. DYKSTRA: Objection. 15 BY MR. BEGLEITER: 16 Q. I'm talking, again, in this 17 period from '97 to 2000. 18 MS. DYKSTRA: Did you say 19 compliance defense? 20 MR. BEGLEITER: That's what I 21 said, compliance defense. 22 THE WITNESS: It depends on your 23 definition of the word "compliance" and 24 it depends on the definition of the 25 word "consult." Because I can define</p>

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<p style="text-align: right;">Page 38</p> <p>1 those in a number of different ways. 2 BY MR. BEGLEITER: 3 Q. Well, did -- was the regulatory 4 group involved with -- at Merck involved with 5 compliance in those years from '97 to '02? 6 A. By definition the regulatory 7 group is involved with compliance, right. 8 Q. And specifically with regard to 9 007? 10 A. Yes. 11 Q. Did you ever -- did they ever 12 come to you and ask you any questions, for any 13 guidance, things like that? 14 MS. DYKSTRA: Object to the 15 form. 16 THE WITNESS: I do not 17 recollect. In terms of specific 18 regulatory guidance, I've given -- but 19 again, you know, that's a very general 20 term, guidance. So if it were general 21 regulatory guidance, no, because they 22 were the experts in regulatory, so why 23 would they come to me for guidance. 24 BY MR. BEGLEITER: 25 Q. Well, would they come to you,</p>	<p style="text-align: right;">Page 40</p> <p>1 which was mine that reported independently 2 into the head of research. 3 Q. When you began in '07 -- excuse 4 me, in '97 with that position in biologics and 5 vaccine, did you -- had MMR II been licensed, 6 as far as you knew? 7 A. MMR II had been licensed for 8 many years prior to that. Decades. 9 Q. Did you know Dr. Hilleman? 10 A. Yes, I had the pleasure of 11 knowing Dr. Hilleman. As a matter of fact, 12 the reason I joined the research laboratories 13 in 1983 is because Dr. Hilleman was the head, 14 had done all the work that he did. My 15 interest was in vaccines. 16 Q. Do you know if in '97 to '02, 17 while you were with the vaccine and biologics 18 research, whether or not Merck had the 19 exclusive license for mumps vaccine in the 20 United States? 21 MS. DYKSTRA: Objection. Form. 22 THE WITNESS: Well, yes. And it 23 still does, I believe, yes. 24 BY MR. BEGLEITER: 25 Q. Eliminate that question.</p>
<p style="text-align: right;">Page 39</p> <p>1 for example, if there was a regulatory 2 question regarding research? 3 MS. DYKSTRA: Objection. 4 THE WITNESS: If there was a 5 regulatory question regarding the 6 activities of events that were going on 7 in laboratories that are responsible to 8 me, yes, they would come to me, of 9 course. 10 BY MR. BEGLEITER: 11 Q. Let me understand how it worked 12 at Merck in those five years. People were 13 collaborative. Is that correct? 14 A. There were independent 15 departments that were responsible for various 16 activities. So if we look within the entire 17 vaccine research effort, the entire vaccine 18 research and development effort included 19 within the overall responsibilities of the 20 research laboratories, included the regulatory 21 group which reported independently into head 22 of regulatory; the clinical research group 23 which reported independently into the head of 24 medical and medical research; and then the 25 research group, the fundamental research group</p>	<p style="text-align: right;">Page 41</p> <p>1 A. Yeah. 2 Q. Do you know if, again, in '97 to 3 '02, whether it perceived a potential 4 competitor for that meaning, if Merck 5 perceived a potential competitor for its 6 exclusive license for MMR II? 7 A. Merck is an institution. 8 Perception is a human endeavor. So I can't 9 answer that question the way you posed it. 10 Q. You can't answer the question 11 what you perceived? 12 A. What I personally perceived? 13 Q. Yes, you're right. I asked if 14 Merck perceived. I'll ask it as you, did you 15 perceive that Merck had a potential competitor? 16 A. I did not perceive that. 17 Q. We discussed Priorix just for a 18 moment or two in relation to another clinical 19 trial. Do you -- what was your understanding 20 in the '97 to '02 time period as to what 21 Priorix was? 22 MS. DYKSTRA: Object to the 23 form. 24 THE WITNESS: Priorix was the 25 GSK version of the vaccine, of Merck's</p>

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<p style="text-align: right;">Page 42</p> <p>1 MMR vaccine. 2 BY MR. BEGLEITER: 3 Q. You understood that Priorix was 4 GSK, GlaxoSmithKline's version, that there 5 was -- did you understand that there was 6 potential competition between the two 7 vaccines? 8 MS. DYKSTRA: Objection. 9 THE WITNESS: Well, there's 10 certainly competition worldwide between 11 the two vaccines, but in the United 12 States I did not perceive that as being 13 a competitive issue. 14 BY MR. BEGLEITER: 15 Q. Were you involved with any kind 16 of research outside the United States? 17 A. Not that I recollect. 18 Q. Let's talk about Dr. Shaw. When 19 did you first meet Dr. Shaw? Approximately, I 20 don't need the exact date. 21 A. I don't recall. Dr. Shaw had 22 been at the company when I joined, when I 23 joined the company. Met him probably very 24 early. 25 Q. And when you became --</p>	<p style="text-align: right;">Page 44</p> <p>1 met Dr. Krah. 2 Q. Do you recollect that he was -- 3 you supervised him during the period of time 4 April '97 -- 5 A. Yes, I do. 6 Q. -- to January 2002? 7 A. Yes, I do. 8 Q. For that entire period? 9 A. As to the best of my recollection. 10 Q. Everything is to the best of 11 your recollection. 12 A. That's true. 13 Q. All right. Now, with regard to 14 Dr. Shaw, going back to Dr. Shaw for a second, 15 did you see him outside of work? Did you 16 socialize? 17 A. Not routinely in those days, no. 18 Subsequent to that, after I had left the 19 company. 20 Q. And how about with Dr. Krah, did 21 you socialize with him? 22 A. Never did. 23 Q. When was the last time you saw 24 Dr. Krah? 25 A. I have not seen Dr. Krah since I</p>
<p style="text-align: right;">Page 43</p> <p>1 A. Or a little bit thereafter. I 2 don't recall exactly. 3 Q. When you became the VP of 4 vaccines and biologics research in '97, was he 5 with that division? 6 A. With the vaccine, yes. With the 7 vaccine research division, yes, he was with 8 that division. 9 Q. Okay. He was with the division 10 when you left that division in January of 11 2002? 12 A. You know, Dr. Shaw also left the 13 company and honestly, I don't recall who went 14 first. I really don't. 15 Q. Would you say, though, that for 16 a good period between April '97 and 17 January 2002 you were supervising Dr. Shaw? 18 A. During that period I was, yes. 19 Q. It may not be to the actual end 20 but for a good period? 21 A. As I said, I don't recall when 22 we got to 2004 who had left first. 23 Q. Let's go to Dr. Krah. Was 24 Dr. Krah -- when did you first meet Dr. Krah? 25 A. I don't recollect when I first</p>	<p style="text-align: right;">Page 45</p> <p>1 left the company, so I can't tell you exactly 2 when, but certainly not since I left the 3 company. 4 Q. Did you ever work on any papers 5 with Dr. Krah? 6 A. There were, I believe, some 7 publications, but I can't -- they would be 8 listed in my CV. I don't remember exactly. 9 It was quite a while. 10 Q. If a paper -- in these years of 11 April '97 to January of '02, were there papers 12 written regarding any clinical trials that you 13 were involved with? 14 A. Within that exact period, again, 15 I don't recollect. We would have to look 16 through my CV, and you will see it. 17 Q. Was there any paper written 18 regarding the trial where the head-to-head 19 competition between Priorix and MMR II? 20 A. I don't recollect. 21 Q. Was there any paper written 22 between -- written regarding Protocol 007's 23 results? 24 A. There may very well have been, 25 but I don't recall -- but I really don't</p>

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1 recall.
 2 Q. Now, when you and Dr. Shaw were
 3 working together sometime during the period of
 4 April to -- '97 to January of '02, how would
 5 you characterize your working relationship
 6 with him?
 7 A. With Dr. Krah, it was a very
 8 formal --
 9 Q. Dr. Shaw.
 10 A. Dr. Shaw, yeah, the same way.
 11 Very formal working relationship. He was one
 12 of my direct reports, and all my direct
 13 reports were very formal relationships.
 14 Q. Did you and Dr. Shaw have
 15 offices in the same building?
 16 A. Yes, next door to each other.
 17 At least during this period, if I remember.
 18 Q. And if he wanted to see you --
 19 withdrawn.
 20 Did you have an open door policy
 21 with regard to him? Could he just come to see
 22 you when he wished?
 23 A. I had a general open door
 24 policy.
 25 Q. In fact, did Dr. Shaw see you

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1 frequently during the time that he worked
 2 there close to the four years?
 3 A. It depends how you define the
 4 word "frequently." Besides I can't -- I don't
 5 know. I mean, obviously there were multiple
 6 interactions between me and Dr. Shaw and all
 7 my direct reports and even other people. You
 8 know, I was there all the time. Most of the
 9 time.
 10 Q. So when you say multiple
 11 interactions, you mean it wasn't a rare event
 12 for you to be seeing Dr. Shaw?
 13 A. It was not a rare event for me
 14 to see anybody who wanted to see me. Certainly
 15 with my direct reports that was true.
 16 Q. Who other than Dr. Shaw was your
 17 direct report in those four years?
 18 A. The ones that I recollect
 19 directly were Dr. John Shiver and Kathrin
 20 Jansen. Those would be two -- among those
 21 three, they ran the three major areas.
 22 Q. How about Peter Kniskern?
 23 A. Peter Kniskern, yes. Actually,
 24 now that you mention his name, I believe I --
 25 I don't formally recollect if he reported

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1 directly to me, but he had -- he did have an
 2 independent operation. He may have, I don't
 3 know.
 4 Q. I'll ask the questions about
 5 Dr. Krah now, the same kind of questions. Was
 6 his office and your office in the same
 7 building?
 8 A. Yes, we were all in the same
 9 building.
 10 Q. How far was his office from your
 11 office?
 12 A. I would have been on a different
 13 floor, because I was on the floor that had the
 14 office areas. So he was laboratory 1, so he
 15 would have been on one of the lab floors.
 16 Q. Your open door policy pertained
 17 to him also. Is that correct?
 18 A. Pertained to anybody.
 19 Q. So if he wanted to speak to you,
 20 did he have to go through a secretary or any
 21 intermediary, any assistant?
 22 A. No. Only insofar if he could
 23 find me or he needed to find me if I wasn't
 24 immediately available.
 25 Q. Would you say that with Dr. Shaw

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1 you had a close working relationship?
 2 A. I had the standard working
 3 relationship that one would have with one's
 4 direct reports.
 5 Q. Did you trust Dr. Shaw?
 6 A. Did I trust Dr. Shaw?
 7 Q. Yes, if he told you something,
 8 did you take it as gospel?
 9 A. It depends. We're scientists,
 10 right, so if he told me a conclusion to
 11 something or statement about something, I
 12 would usually ask for the supporting data.
 13 Q. But if he told you a fact, like
 14 a fact regarding personnel, for example, would
 15 you trust his statement?
 16 A. No, particularly when it comes
 17 to -- again, everything. It's such a science,
 18 it's everything, right. You always need
 19 supporting data, right. So if someone comes,
 20 and it doesn't matter who it is, and tells me
 21 a fact, I always ask for the supporting
 22 information. Or if it's not immediately
 23 available and if it's an important fact to
 24 determine -- that I would like to really
 25 determine if it is a fact, I will ask -- I

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<p style="text-align: right;">Page 50</p> <p>1 will go find the supporting data. 2 Q. And did you ever find -- do you 3 recall anything he ever told you that turned 4 out to be unreliable? 5 MS. DYKSTRA: Objection. 6 THE WITNESS: No. I don't 7 recollect anything like that. 8 BY MR. BEGLEITER: 9 Q. Let's go to Dr. Krah now for a 10 second. I take it -- I'll ask the question. 11 Did you respect Dr. Shaw? 12 A. Yes, I respected Dr. Shaw. I 13 respected everyone. 14 Q. Let's go to Dr. Krah. Did he 15 ever tell you anything that you found to be 16 unreliable? 17 A. No, not to my recollection. 18 Q. And did you respect him? 19 A. As I said, I respected everyone 20 who worked for me. 21 Q. Is there anybody that ever 22 worked for you that did something that you 23 lost respect for them? 24 A. No, because that would have 25 probably -- losing respect for me means</p>	<p style="text-align: right;">Page 52</p> <p>1 expiry potency in healthy children 12 to 2 18 months of age? Do you recognize those 3 words? 4 A. Yes, I do. 5 Q. What do you recognize them as? 6 A. I recognize them as what would 7 likely have been the title of Protocol 007. 8 Q. Sitting here today, do you 9 understand what the purpose of Protocol 007 10 was? 11 A. Sitting here today and 12 subsequent to the review of the documents over 13 the last period of time, yes. 14 Q. And what was that purpose or 15 purposes? 16 A. The original purpose, to my 17 recollection, of the study was to determine 18 whether or not the vaccine, if administered to 19 children at various what were, used to be 20 so-called potencies of the vaccine which would 21 have reflected the amount of actual vaccine 22 virus that is in the vaccine, raised 23 potencies, were capable of eliciting immune 24 responses that were reflective of the immune 25 response, that were reflective of the immune</p>
<p style="text-align: right;">Page 51</p> <p>1 essentially doing something which is overtly 2 wrong. And that I did not, to my 3 recollection, see anything like that in those 4 years, or for that matter any subsequent years 5 or any previous years. 6 Q. Did you trust Dr. Krah's ability 7 to keep you informed of essential goings on in 8 the lab? 9 A. He would have kept Dr. Shaw 10 informed who, in turn, would have kept me 11 informed. 12 Q. So if Dr. Krah told Dr. Shaw 13 something important, you would expect at least 14 Dr. Shaw to tell you? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: If Dr. Shaw 17 perceived it to be at the same level of 18 importance and supportable. 19 BY MR. BEGLEITER: 20 Q. Let me ask you a question. Do 21 you recall the official title of Protocol 007? 22 A. No, I don't. I did not review 23 the protocol. 24 Q. What about, do you recognize the 25 following words, a study of MMR at mumps</p>	<p style="text-align: right;">Page 53</p> <p>1 response that would be elicited by the 2 vaccine, and to determine whether or not those 3 immune responses were equivalent at -- I 4 believe there were several levels of potencies 5 that were tested in the study. 6 Q. And it was the expiry potencies 7 that were being looked at. Is that correct? 8 A. Well, the study was designed to 9 evaluate three different potencies. Now, 10 would they -- how they related to the 11 potential of their being declared as expiry 12 potencies was part of the entire larger 13 question that was being addressed. 14 Q. Was one of the potencies that 15 was being looked at the current potency at the 16 time of MMR II? 17 A. The current expiry potency? 18 Q. Well, the current potency, let's 19 say release potency? 20 A. Well, no. To my recollection, 21 the three potency levels that were being 22 assessed were being assessed as potential -- 23 at expiry potency levels. So one of them 24 would have been one that would have been 25 reflective of the vaccine in circulation at</p>

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1 the time.
 2 Q. And that -- do you recall what
 3 the potency level was of that, of the vaccine
 4 as --
 5 A. I don't know.
 6 Q. You mentioned now a few times
 7 there are three potencies.
 8 A. There were three potencies, 4.3,
 9 4.1 and 3.7.
 10 Q. 4. --
 11 A. 4.3, 4.1 and 3.7. Again, that
 12 was from my review of the documents.
 13 Q. Knowing what you know, was one
 14 of those potencies the potency on the label?
 15 A. The label at the time indicated,
 16 and what raised the question to begin with,
 17 the label that had been present since the
 18 virus -- since the vaccine, rather, had been
 19 originally licensed was a potency level of, I
 20 believe it was 4 -- it was the 4.3 potency
 21 level. But what the label said -- again, upon
 22 my review of that original label, it said that
 23 the vaccine contains, you know, 4.3 logs of
 24 mumps virus.
 25 Q. When you became involved with

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1 Protocol 007, was -- did anyone communicate to
 2 you from Merck that there was a desire to
 3 lower the labeled potency?
 4 A. Not that there was a direct
 5 desire to lower the label potency but rather
 6 to determine if the -- what were likely to be
 7 the end of shelf life potencies, which would
 8 be, of course, the expiry potency, were
 9 potencies that were capable of eliciting
 10 immune responses that would be -- again,
 11 remember the assays that one uses are indirect
 12 measures of immune responses -- rather
 13 indirect measure of what the effect of an
 14 immune response might be, it's not the direct
 15 measure. But to determine whether or not
 16 there were equivalent abilities to elicit
 17 immune responses to the vaccine.
 18 Q. Okay. But was -- I understand
 19 that, but I'm asking whether or not anybody
 20 told you that they wanted to change the label
 21 potency?
 22 MS. DYKSTRA: Objection to form.
 23 BY MR. BEGLEITER:
 24 Q. This is, again, the period '97
 25 to '01.

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1 A. Not to change the question, The
 2 question is too broad. So it's difficult for
 3 me to answer which is why I'm hesitating here.
 4 The label potency, so are you referring to
 5 expiry potency or the release potency? It
 6 depends. They're two different things.
 7 Q. Did the label, when you were at
 8 Merck, have an expiry potency on it?
 9 A. The label had a potency on it.
 10 What had -- potency. The question as to
 11 whether or not it should be the expiry --
 12 formally established as the expiry potency,
 13 that number was a question that had been
 14 raised by the FDA in previous discussions.
 15 Q. So did Merck, as far as you
 16 know, take the position that that 4.3 was good
 17 enough, was a good number for the potency of
 18 the vaccine at expiry?
 19 A. Its position was that that
 20 number was good enough at expiry and probably
 21 also good enough at original release. Because
 22 the way the original label was written
 23 suggested, this goes back decades, suggested
 24 that that number was reflective of the amount
 25 of vaccine virus that was used to actually

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1 produce the vaccine.
 2 Q. Do you know how much virus was
 3 used to produce the vaccine?
 4 MS. DYKSTRA: Objection to form.
 5 THE WITNESS: No, I don't other
 6 than what it says. So if I were to
 7 read the label at face value, what goes
 8 in is -- when it was originally
 9 developed was approximately 4.3 logs of
 10 mumps virus.
 11 BY MR. BEGLEITER:
 12 Q. What is -- well, let me ask, do
 13 you know what 4.3 logs comes to in terms of
 14 units?
 15 A. 4.3 logs, four logs would be
 16 10,000, so that would be roughly 20,000.
 17 Q. One less document to look at.
 18 So approximately 20. Is the
 19 scientific way of referring to it, would that
 20 be -- of the 4.3, would that be 4.3 log 10
 21 TCID50?
 22 A. So that would be 4.3 log to the
 23 base ten, because there are multiple logs that
 24 are not base ten, but that's log to the base
 25 10, tissue culture, 50 percent tissue culture

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<p style="text-align: right;">Page 58</p> <p>1 effective doses. 2 Q. Let's return to the 006 -- 3 excuse me, to the head to head, the Priorix 4 versus MMR II. Do you know why that study was 5 conducted? 6 A. I don't recollect. 7 Q. Do you know what the results 8 were? 9 A. I do not recollect directly. 10 Q. Do you know if they were 11 published? 12 A. I don't recollect. 13 Q. Do you recall who won in that 14 head to head? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: I don't recollect 17 the results. 18 BY MR. BEGLEITER: 19 Q. I'm not asking specific results, 20 I'm asking just a general question. Did 21 either one of them turn out to be a better one 22 than the other? 23 A. I don't recollect. I really 24 don't. 25 Q. Were you involved with budgets</p>	<p style="text-align: right;">Page 60</p> <p>1 in collaboration of this, yes. 2 Q. Were there contracts with these 3 outside laboratories? 4 A. It depended on the nature of the 5 study. It could have been research 6 collaborations, it could have been contracts 7 to do specific work. 8 Q. Do you know whether there was a 9 contract, whether an outside lab did work on 10 that head-to-head study of Priorix and MMR II? 11 A. I don't recollect. 12 Q. When Merck retains an outside 13 lab -- withdrawn. 14 Were you involved ever with 15 determining whether an outside lab should be 16 used in a Merck study? 17 A. I don't recollect in the context 18 of MMR II or within this time, but other 19 points of my responsibility there I was 20 involved, yes. 21 Q. What criteria, if you know, were 22 used by Merck to determine whether or not -- 23 let me finish -- whether or not an outside 24 laboratory was competent? 25 A. It depended on the work that</p>
<p style="text-align: right;">Page 59</p> <p>1 at all? 2 A. Only with regard to the budgets 3 in my own department. 4 Q. Did you -- was there a budget 5 for Protocol 007? 6 A. That would not have been in my 7 responsibility. My responsibility were the 8 budgets of the overall department. I would 9 not have been responsible for the budgets of a 10 specific study. 11 Q. Who would have been? 12 A. The medical research group. 13 Q. And who was in charge of that 14 then, do you know? 15 A. I honestly don't recall. 16 Q. Did you ever review the budget? 17 MS. DYKSTRA: Objection. 18 THE WITNESS: No, I would not -- 19 not just -- normally, I would not 20 review the budget of a clinical study. 21 BY MR. BEGLEITER: 22 Q. While you were at Merck, would 23 outside labs ever do work for Merck? 24 A. That was routine practice. 25 Outside laboratories would do various studies</p>	<p style="text-align: right;">Page 61</p> <p>1 needed to be done. 2 Q. How would Merck go about doing 3 the analysis? 4 A. It would depend on the work that 5 needed to be done and an assessment would 6 probably be performed of the laboratory and -- 7 to make sure that it would maintain the 8 appropriate standards, generated reproducible 9 data. Typical. 10 Q. Merck wouldn't contract with an 11 outside laboratory, as far as you know, that 12 was incompetent? 13 MS. DYKSTRA: Objection. 14 THE WITNESS: Of course not. 15 BY MR. BEGLEITER: 16 Q. Or lacked integrity? 17 A. Of course not. 18 Q. Was not professional? 19 A. Of course not. 20 Q. Now, you mentioned a few moments 21 ago that there was this difference of opinion 22 between Merck and the FDA regarding the end 23 expiry potency that was on the label? 24 MS. DYKSTRA: Objection. 25 THE WITNESS: To the best of my</p>

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<p style="text-align: right;">Page 62</p> <p>1 recollection, it was not a difference 2 of opinion. What it was was that the 3 label indicated that the potency of the 4 vaccine was 4.3 logs of mumps. The 5 vaccine like every pharmaceutical 6 product has a shelf life. The agency's 7 position in the late 1990s was, and 8 this was at a time that they were 9 reviewing their internal rules and 10 regulations, took the position that 11 what was listed on the label as the 12 potency needed to reflect the potency 13 at the end of shelf life, hence the 14 expiry potency. 15 BY MR. BEGLEITER: 16 Q. Do you know what the shelf life 17 of MMR II was? 18 A. I believe it was approximately 19 24 months at the time. I believe. I don't 20 recall directly, to be honest. 21 Q. When you say "approximately," 22 you mean because you're not 100 percent sure 23 or because -- 24 A. No, it's because I'm not 100 25 percent certain. Normally the shelf life</p>	<p style="text-align: right;">Page 64</p> <p>1 Merck challenged that mandate, that conclusion 2 of the FDA? 3 MS. DYKSTRA: Objection. Form. 4 THE WITNESS: I don't think 5 anyone necessarily challenged it. I 6 think that what it was was a question 7 that came up which said simply that if 8 now this number of 4.3 is to be 9 considered the end expiry potency and, 10 of course, given that, just like any 11 pharmaceutical product, the product 12 does decay over time, it's second law 13 of thermodynamics, does decay over time 14 on storage, then the question is, you 15 know, is the end expiry potentially 16 somewhat less than 4.3. We don't know. 17 And, therefore, should the number be, 18 in fact, lower to really represent end 19 expiry potency. 20 BY MR. BEGLEITER: 21 Q. First of all, when you were 22 dealing with the FDA, was there a specific 23 division of the FDA that you would deal with? 24 A. The division at the FDA was the 25 old division that was referred to as the</p>
<p style="text-align: right;">Page 63</p> <p>1 would be -- it wouldn't be 23 months, it would 2 be 24 months or 36 months, something of that 3 nature. 4 Q. The people at the FDA that 5 you -- that would be -- withdrawn. 6 There was a question, if I used 7 the word before, there was a question about 8 whether the 4.3 met the FDA's requirement of 9 end expiry potency? 10 MS. DYKSTRA: Objection to the 11 form. 12 THE WITNESS: Whether it met 13 FDA's new perception of what that 14 number should mean. Because prior to 15 that time, there was no question at all 16 with regard to what 4.3 logs refer to. 17 It was only when we got to the point of 18 there being an indication that the 19 agency said, you know, this number 20 should really reflect end expiry 21 potency. That was the change that 22 happened. 23 BY MR. BEGLEITER: 24 Q. That's what they said, but I 25 want to know if you're aware that anyone at</p>	<p style="text-align: right;">Page 65</p> <p>1 Bureau of Biologics, then became known as the 2 Center for Biologics, Evaluation and Research. 3 It's the same division that is responsible 4 today for vaccines. 5 Q. And that Center for Biologics 6 was known colloquially as CBER? 7 A. Center For Biologics, 8 Evaluations and Research, CBER. That's right. 9 Q. Okay. So just to be clear, I 10 think you've touched it, but let's make it 11 clear, the question was, at end expiry, 12 whether or not the vaccine had 20,000 base ten 13 TCID50? Isn't that really the question? 14 A. No. Just to take a step back, 15 the label of the vaccine from the day it was 16 first licensed many decades ago indicated that 17 the amount of virus in the vaccine was 20 -- 18 for mumps was 20,000 TCID50. There was no 19 indication in the label as to whether that was 20 the end expiry number or the release number. 21 So, in fact, one could argue it either way, 22 that the vaccine had to have at least 20,000 23 on the day it left the factory or had to have 24 20,000 on the day it could no longer be used 25 because it achieved the end of shelf life.</p>

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<p style="text-align: right;">Page 66</p> <p>1 Q. And then --</p> <p>2 MS. DYKSTRA: Can he finish?</p> <p>3 BY MR. BEGLEITER:</p> <p>4 Q. I'm sorry, I thought you were</p> <p>5 finished.</p> <p>6 A. No. So the agency, taking a</p> <p>7 conservative position at that time in the late</p> <p>8 1990s, said that number should reflect the end</p> <p>9 expiry potency. It was a declaration by the</p> <p>10 agency. There was no data at that time to</p> <p>11 support whether or not vaccine that contained,</p> <p>12 actually contained less than 20,000 at end</p> <p>13 expiry would not be effective. There was no</p> <p>14 data to support that. It was simply a</p> <p>15 declaration.</p> <p>16 Q. Now, the declaration of 20,000</p> <p>17 TCID50 --</p> <p>18 A. At end expiry.</p> <p>19 Q. -- at end expiry, CBER wanted to</p> <p>20 know if that was true. Isn't that right?</p> <p>21 MS. DYKSTRA: Objection.</p> <p>22 THE WITNESS: What do you mean</p> <p>23 by "true"?</p> <p>24 BY MR. BEGLEITER:</p> <p>25 Q. In other words, that was what --</p>	<p style="text-align: right;">Page 68</p> <p>1 my recollection, but -- no, not to my</p> <p>2 recollection. But it depends, again, what you</p> <p>3 defined as end expiry trials. In the</p> <p>4 development of any pharmaceutical substance,</p> <p>5 there are studies that are conducted, you</p> <p>6 know, certainly in current last period of</p> <p>7 time. Let's go back to, let's call it the</p> <p>8 last 20 years. There are studies that are</p> <p>9 typically conducted to determine what should</p> <p>10 be the end expiry potency, however you define</p> <p>11 potency, in the label. But that was not the</p> <p>12 standard going back certainly to the 1960s and</p> <p>13 early 1970s.</p> <p>14 Q. Well, are you aware -- there's</p> <p>15 no doubt that Protocol 007 was an end expiry</p> <p>16 study. Right?</p> <p>17 A. That was to answer a very</p> <p>18 specific question, which was, what would the</p> <p>19 potency of the -- what would the immunological</p> <p>20 potency of the vaccine be. That's what that</p> <p>21 study was designed to measure. What was the</p> <p>22 immunological potency of the vaccine at levels</p> <p>23 that were below 4.3.</p> <p>24 The vaccine was -- there was</p> <p>25 never a question by the agency or by Merck as</p>
<p style="text-align: right;">Page 67</p> <p>1 if one tested the vaccine, one would find</p> <p>2 20,000 TCID50?</p> <p>3 MS. DYKSTRA: Objection.</p> <p>4 THE WITNESS: No, that's not to</p> <p>5 my recollection as to whether or not</p> <p>6 that question came up. The question</p> <p>7 that came up was whether or not the</p> <p>8 vaccine would retain potency at what --</p> <p>9 that the potency that was present at</p> <p>10 20,000 was also retained at levels</p> <p>11 below 20,000, on the assumption that if</p> <p>12 20,000 was considered to be the release</p> <p>13 potency, that there was a likelihood</p> <p>14 that at the end of the shelf life, this</p> <p>15 effective vaccine would contain less</p> <p>16 than 20,000 so, therefore, what is that</p> <p>17 number, so that one could actually put</p> <p>18 an end expiry number in the label that</p> <p>19 was reflective of the actual potency of</p> <p>20 an effective vaccine.</p> <p>21 BY MR. BEGLEITER:</p> <p>22 Q. During your time at Merck in the</p> <p>23 biologic and -- vaccine biologics research,</p> <p>24 had there been any other end expiry trials?</p> <p>25 A. Not -- had there been? Not to</p>	<p style="text-align: right;">Page 69</p> <p>1 to whether or not the vaccine that was being</p> <p>2 used was effective or not. It was effective.</p> <p>3 The question was, okay, what level is still --</p> <p>4 what level should be present, what level, what</p> <p>5 potency level, use that terminology, should</p> <p>6 still be present in the vaccine at the end of</p> <p>7 shelf life that reflects the effectiveness of</p> <p>8 the vaccine. Because remember, 4.3 was simply</p> <p>9 a declaration, not based on data.</p> <p>10 It was known that the vaccine at</p> <p>11 4.3 was effective because it was originally</p> <p>12 designed to have 4.3 in it at release and,</p> <p>13 therefore, that was what probably was present</p> <p>14 at the time that the efficacy studies were</p> <p>15 ongoing, but there was no evidence of any loss</p> <p>16 of efficacy over time.</p> <p>17 Q. Let's maybe have some</p> <p>18 definitions. What is immunological potency?</p> <p>19 A. Immunological potency is -- so</p> <p>20 when immunological potency, the question -- so</p> <p>21 let's do it -- it's a broad question. So</p> <p>22 we'll do it in the context of the 007 trial.</p> <p>23 The 007 trial was designed to</p> <p>24 determine whether or not different levels of</p> <p>25 the vaccine or the vaccine produced that</p>

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<p style="text-align: right;">Page 70</p> <p>1 contained different levels of the mumps virus, 2 right, 4.3, 4.1, 3.7 logs, were capable, were 3 each capable of equivalently eliciting immune 4 responses as measured, that's a key point, as 5 measured, that were reflective of the immune 6 response that would be elicited by the 7 vaccine. 8 Q. Can you give me a definition of 9 what you mean by "efficacy"? 10 A. Efficacy has a very specific 11 definition. It is whether or not -- well, 12 again, it depends the context of the product. 13 But in the context of a vaccine is whether or 14 not the vaccine, okay, is effective in a 15 clinical setting to prevent disease caused by 16 the pathogen against which the vaccine is 17 designed to be effective. 18 Q. Now, let me just see if I 19 understand what you said about the direction 20 from the FDA, from CBER. Are you saying that 21 CBER had no scientific basis, at the time that 22 007 was begun, to direct that Merck have 23 this -- have 4.3 TCID whatever at expiry? 24 TCID50, I'm sorry. Because you said a couple 25 of times --</p>	<p style="text-align: right;">Page 72</p> <p>1 was something -- this was a general 2 concern that had arisen within the 3 agency around this time, not just 4 related to mumps but to every other 5 product that they were responsible for 6 regulating over the issue of control. 7 How do you know that the product that 8 you make is the same all the time and 9 how do you know that the product that 10 you use, that includes the product all 11 the way up to the end of expiry, is the 12 same all the time with regards 13 primarily to its efficacy. 14 BY MR. BEGLEITER: 15 Q. How do you know the -- how do 16 you know that the FDA was requiring this in 17 more than MMR II? 18 A. This was across the industry. 19 These questions came up across the industry 20 with regards to how does one tighten the 21 language in the label, how does one tighten 22 manufacturing control processes, you know, 23 because there were many issues, and which 24 were, again, across the industry in general, 25 roughly around this time, late 1990s, early</p>
<p style="text-align: right;">Page 71</p> <p>1 A. Please be more specific in your 2 question. 3 Q. Well, I believe you said that 4 the FDA was acting conservatively -- 5 A. Right. 6 Q. -- when they required this end 7 expiry study. And I'm asking you whether or 8 not there was any scientific reason, health 9 reason, medical reason to do it? 10 MS. DYKSTRA: Objection to form. 11 THE WITNESS: To my knowledge, 12 to my knowledge, and based upon the way 13 in which the questions were asked, the 14 study was conducted and subsequent 15 discussions, you know, between the 16 agency and the company, the agency did 17 not have a reason to declare 4.3 as a 18 requirement because of fear that there 19 would be loss of efficacy or that the 20 vaccine was not efficacious at levels 21 less than 4.3. There's no evidence for 22 that. 23 The reason why the agency 24 declared end expiry should be 4.3 was 25 because the agency was concerned, this</p>	<p style="text-align: right;">Page 73</p> <p>1 2000s. And as a result, language needed to be 2 tightened in the labels. This is an example 3 of that. Additional control processes needed 4 to be put into place during manufacturing for 5 a whole number of other vaccines. This was, 6 again, and it wasn't -- I just want to make 7 the point, it wasn't Merck specific, it was 8 industry specific. 9 Q. Can you name other vaccines that 10 were required to tighten up their labels? 11 A. Well, not just tighten up their 12 labels but tighten up general controls in 13 general. I will tell you that there was a 14 major, a major turnover of the vaccine 15 industry in those days as a result of the 16 agency insisting on tighter perspectives. 17 There were vaccines that were marketed that 18 were taken off the market. None of them being 19 Merck. Other companies, and we won't go into 20 those details. 21 Q. Can you name a vaccine that 22 was -- where label was tightened and controls 23 were tightened in this period because of this 24 agency effort? 25 A. I can't name one directly off</p>

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<p>1 the top of my head, but it was general 2 activity that was ongoing. 3 Q. Do you know what level of 4 immunogenicity that was required of the MMR II 5 vaccine? 6 MS. DYKSTRA: Objection. 7 THE WITNESS: So, again, not 8 that I recall at the time itself but in 9 reviewing the documents over the last 10 several periods of time, what the 11 agency was looking for was looking for 12 an immunological assay that was capable 13 of showing that the vaccine, when used 14 at what they were now calling the end 15 expiry value of 4.3, would be able to 16 demonstrate at least a 90 percent 17 seroconversion. 18 BY MR. BEGLEITER: 19 Q. Was that 90 percent including a 20 5 -- including some -- 21 A. Variance. 22 Q. Some -- I'm trying to think of 23 the word. Some confidence interval? 24 A. Confidence interval. It's in 25 the report here. Confidence interval which is</p>	<p>1 occurred.) 2 - - - 3 BY MR. BEGLEITER: 4 Q. I've shown you Merck KRA01449029 5 through 9040, and ask you what this document 6 is, if you know? 7 A. This appears to be the label or 8 what is also referred to as the package insert 9 for MMR II. What I cannot tell by just 10 looking at it is which year this package 11 insert came from. 12 Q. Let me -- if you go right to the 13 very end, the very end, page 12. 14 A. Issued date is April 1999. 15 Thank you. 16 Q. All I'm going to ask you about 17 this document is the -- is what the label said 18 about the seroconversion rate for the mumps 19 component of MMR II. And if you go to the 20 carryover paragraph from page 1 to page 2, I 21 think that might have the answer. 22 MS. DYKSTRA: I'm sorry, do you 23 want him to identify anywhere the label 24 talks about seroconversion rate? 25 MR. BEGLEITER: No, I'm asking</p>
Page 75	Page 77
<p>1 the variance. 2 All biological assays and all 3 assays in general by definition have 4 confidence intervals. 5 Q. So the 90 percent was with the 6 confidence? 7 A. 90 percent would have been the 8 point estimate. You would then -- point 9 estimate being the midpoint of the confidence 10 interval. 11 Q. Do you recall what the label 12 said about the -- 13 A. I do not recall what the label 14 said. 15 MS. DYKSTRA: When -- Bob, when 16 you get a chance to take a break either 17 before or after you finish -- 18 MR. BEGLEITER: This is a one 19 minute. 20 - - - 21 (Exhibit Emini-2, MMR II package 22 insert, 01449029 - 01449040, was marked 23 for identification.) 24 - - - 25 (A discussion off the record</p>	<p>1 him just basically to refresh his 2 recollection. 3 THE WITNESS: Okay. 4 BY MR. BEGLEITER: 5 Q. Just ask you, having read the 6 carryover sentence -- 7 A. Yes, I have. 8 Q. -- is your recollection refreshed 9 as to the SCR required of the vaccine? 10 MS. DYKSTRA: Objection. 11 THE WITNESS: This is not the 12 SCR that is required. What it says 13 here is that, very clearly, that 14 "Clinical studies of 279 triple 15 seronegative children...," and I'm 16 reading the paragraph, "...11 months to 17 7 years of age, demonstrated that MMR 18 II is highly immunogenic and generally 19 well tolerated. In these studies, a 20 single injection of the vaccine induced 21 measles...," and then it tells you the 22 measles, but I'll refer to the mumps, 23 "...mumps neutralizing antibodies in 24 96 percent...of susceptible persons." 25 That is simply a report of what was</p>

20 (Pages 74 - 77)

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<p style="text-align: right;">Page 78</p> <p>1 observed in the clinical study that is 2 being referenced. It is not a 3 requirement. 4 BY MR. BEGLEITER: 5 Q. But this document, is this an 6 insert for the vaccine? 7 A. Yes, it is. 8 Q. And this, as far as you know, is 9 given to every medical center, physician who -- 10 A. Whoever purchases the vaccine 11 gets an insert because it's in the box. 12 Q. And when you answered 90 percent 13 before, what were you reserving to there? 14 A. I was referring specifically to 15 the context of the 007 clinical trial and what 16 the agency, the FDA was looking for in terms 17 of the quality of the assay that was being 18 used to assess the immunological response to 19 the vaccine. That's a different situation 20 than what's in the label here. This label is 21 reporting data from its original efficacy 22 study. We need to recall that what you 23 measure is a function of how you measure it. 24 That the assay that was used back when this 25 clinical study was originally conducted, and,</p>	<p style="text-align: right;">Page 80</p> <p>1 what 007 was, of the ability of the vaccine at 2 three different dosage levels, its ability to 3 elicit a seroconversion response in young 4 children, one wants as sensitive a vaccine as 5 possible -- excuse me, as sensitive an assay 6 as possible. If the vaccine were not capable 7 of eliciting a seroconversion of at least 90 8 percent given the assay that you developed, 9 you wouldn't be able to tell the difference 10 between 90 percent or a few percentage points 11 later, because typically the lower the 12 midpoint of what you measure, the wider the 13 confidence intervals and it becomes difficult 14 to discern what's happening. 15 Q. Just to be straightened out, the 16 90 percent you're talking about is pre the 17 confidence interval or post the confidence 18 interval? 19 A. No, I view it as -- I interpret 20 it as the midpoint of the confidence interval. 21 Q. So in other words, it could be 22 from 95 to 85? 23 A. If the confidence interval -- 24 Q. If it were 5 percent. 25 A. -- were 5 percent, it would be</p>
<p style="text-align: right;">Page 79</p> <p>1 again, I need -- I don't know if it's 2 appropriately referenced here so we can go 3 back to see when the study was originally 4 conducted, we'll have to read and take a look 5 at it, but I'm certain it was many decades 6 before the late 1990s because that was when 7 the vaccine was first licensed. That assay 8 was no longer in existence by the time of the 9 007 study. So a new assay had to be developed 10 and the agency wanted the assay to be 11 sensitive. What I mean by sensitivity, it 12 needed to be able to discern a difference in 13 the seroconversion rate that could be elicited 14 by 4.3, 4.1 and 3.7. Those were the three 15 comparators, right, that were being done. It 16 had nothing to do with what was originally 17 done many decades ago. 18 Q. So the 90 percent you're talking 19 about which is post the confidence interval -- 20 A. No, the 90 percent is, I 21 presume, but the 90 percent, because in the 22 documents I saw the number that I recollect 23 was 90 percent, 90 percent is a measure of the 24 assay sensitivity. So, for instance, if one 25 wants to look at -- do a comparison, which is</p>	<p style="text-align: right;">Page 81</p> <p>1 referred to as 90 percent plus or minus 5 2 percent. 3 MR. BEGLEITER: We can have our 4 break. 5 VIDEOGRAPHER: The time is 6 10:54. Going off the video record. 7 - - - 8 (A recess was taken.) 9 - - - 10 VIDEOGRAPHER: The time is 11 11:09. We're back on the video record. 12 MS. DYKSTRA: Dr. Emini, you 13 asked him about the different arms in 14 the 007 study and what the potencies 15 were in the different arms. I think 16 you may want to clarify what they were. 17 He didn't have anything in front of him 18 at the time, but he can clarify. 19 THE WITNESS: I mentioned they 20 were 4.3, 4.1, 3.7. My apologies. The 21 levels that were being tested were 4.9, 22 4.0 and 3.7. 23 BY MR. BEGLEITER: 24 Q. Now, in going back to the 25 seroconversion rate for a moment, was -- did</p>

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<p style="text-align: right;">Page 82</p> <p>1 CBER ever communicate to you that they were</p> <p>2 looking for a 95 percent seroconversion rate?</p> <p>3 A. To me?</p> <p>4 Q. Yes.</p> <p>5 A. No, there was no communication.</p> <p>6 Q. Were you ever told by anyone at</p> <p>7 Merck that they were looking -- that CBER was</p> <p>8 looking for 95 percent seroconversion rate?</p> <p>9 A. Not at all to my recollection.</p> <p>10 Q. Now, when Protocol 007 was in</p> <p>11 development, did a decision have to be made</p> <p>12 about which strain of mumps vaccine -- which</p> <p>13 strain of mumps virus was going to be used for</p> <p>14 the assays?</p> <p>15 A. Yes.</p> <p>16 Q. And do you recall sitting here</p> <p>17 today what the candidates were for -- let me</p> <p>18 finish the question -- for the strain for the</p> <p>19 protocol?</p> <p>20 A. For the assays?</p> <p>21 Q. For the assays.</p> <p>22 A. For the assays and protocol.</p> <p>23 There were two assays, one was a plaque</p> <p>24 reduction neutralization assay, the other was</p> <p>25 an ELISA assay as I said previously. Just so</p>	<p style="text-align: right;">Page 84</p> <p>1 assay was capable of measuring a seroconversion</p> <p>2 rate that would be then statistically capable</p> <p>3 of determining a difference in seroconversion</p> <p>4 among the three levels of vaccine potency that</p> <p>5 were being tested in the protocol.</p> <p>6 Q. But they weren't interested in</p> <p>7 the end result, they were interested only in</p> <p>8 the differences?</p> <p>9 A. They were interested in the</p> <p>10 differences because that was the critical</p> <p>11 aspect. The three levels of potency that were</p> <p>12 being tested give rise to three -- if they</p> <p>13 would, would they give rise to three different</p> <p>14 seroconversion levels.</p> <p>15 Q. Can you name any of the wild</p> <p>16 type vaccines -- excuse me, any of the wild</p> <p>17 type strains of mumps that were available?</p> <p>18 A. No, I don't recollect them off</p> <p>19 the top of my head. The only one I can name</p> <p>20 is the one that was in actual use for the</p> <p>21 assay itself.</p> <p>22 Q. And what was the name of that?</p> <p>23 A. That was referred to as a low</p> <p>24 passage Jeryl Lynn strain.</p> <p>25 Q. And that was the strain that was</p>
<p style="text-align: right;">Page 83</p> <p>1 we're clear, we're always talking two assays</p> <p>2 here.</p> <p>3 No, I don't recall what the</p> <p>4 candidates were other than the fact, and</p> <p>5 again, this came from my review over the last</p> <p>6 period of time of documents, other than the</p> <p>7 fact that the candidate had to be a so-called</p> <p>8 wild type virus. It could not be the vaccine</p> <p>9 virus itself.</p> <p>10 Q. And were assays taken</p> <p>11 preliminarily of some of the wild type</p> <p>12 viruses?</p> <p>13 MS. DYKSTRA: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I don't recollect</p> <p>16 the details of any work that was done</p> <p>17 along those lines.</p> <p>18 BY MR. BEGLEITER:</p> <p>19 Q. And just, again, if you don't --</p> <p>20 with regard to these wild type viruses, was</p> <p>21 there an expectation from CBER as to what the</p> <p>22 seroconversion rate would be for those wild</p> <p>23 type viruses?</p> <p>24 A. To my recollection, the only</p> <p>25 thing that CBER wanted to see was that the</p>	<p style="text-align: right;">Page 85</p> <p>1 used by Dr. Hilleman to come up with the mumps</p> <p>2 vaccine?</p> <p>3 MS. DYKSTRA: Objection.</p> <p>4 THE WITNESS: So that was the --</p> <p>5 it was -- no, it wasn't the exact one.</p> <p>6 This was a low passage Jeryl Lynn</p> <p>7 strain. So this was -- the way in</p> <p>8 which this was done is that the virus</p> <p>9 was originally isolated from Jeryl</p> <p>10 Lynn, who happened to be Dr. Hilleman's</p> <p>11 daughter actually, from -- was isolated</p> <p>12 from Jeryl Lynn and became known as the</p> <p>13 Jeryl Lynn virus. Then the virus was</p> <p>14 then passaged in cell cultures many,</p> <p>15 many, many times to attenuate it, in</p> <p>16 other words, to make it less capable of</p> <p>17 causing disease but yet still eliciting</p> <p>18 an immune response. I do not recall</p> <p>19 the exact passage of the Jeryl Lynn</p> <p>20 virus that then became the exact strain</p> <p>21 that is used in the vaccine. The low</p> <p>22 passage version was considered to be,</p> <p>23 appropriately so, a wild type virus,</p> <p>24 because of the low passage that was</p> <p>25 used for the purposes of the vaccine,</p>

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<p style="text-align: right;">Page 86</p> <p>1 it was a virus that if one, in fact, 2 put it into a child would more likely 3 than not actually cause disease. 4 BY MR. BEGLEITER: 5 Q. To be clear, the Jeryl Lynn 6 strain was the strain from which the mumps 7 vaccine was developed. Isn't that right? 8 A. The Jeryl Lynn isolate, not the 9 strain, isolate, was the isolate from which 10 the vaccine was eventually developed. The 11 exact strain that was used is a reflection of 12 both the isolate, where it came from, hence 13 Jeryl Lynn, and how many passages it had 14 undergone in cell culture to attenuate it to 15 make it the vaccine strain. So a low passage 16 Jeryl Lynn strain is very different than the 17 Jeryl Lynn vaccine strain. 18 Q. And was there a consideration of 19 something called a cytopathic effect 20 neutralization test being used as an assay? 21 A. Well, the way in which the 22 neutralization assay was performed is that one 23 takes the indicator virus, which in this case 24 was the low passage Jeryl Lynn strain, one 25 places it on a sheet of cells. The virus --</p>	<p style="text-align: right;">Page 88</p> <p>1 was -- I don't recollect the exact 2 details of the discussions. What I can 3 say is that both assays were used, the 4 plaque reduction neutralization assay 5 and the ELISA assay. To be clear, the 6 selection of the assays were not 7 conducted by Merck alone but was always 8 in collaboration with the FDA, because 9 the purpose was to answer a very 10 specific question that the FDA asked us 11 to answer and, therefore, it was a 12 decision made by both organizations. 13 BY MR. BEGLEITER: 14 Q. Who ran the PRN test for 15 Protocol 007? 16 A. So the PRN test was being run in 17 David Krah's -- was developed and run in David 18 Krah's laboratory. 19 Q. Who ran the ELISA test for 20 Protocol 007? 21 A. I actually don't recollect if 22 that was in David Krah's laboratory or a 23 separate laboratory. That, I don't recollect 24 clearly. 25 Q. Did you have an understanding --</p>
<p style="text-align: right;">Page 87</p> <p>1 Q. It's all right if you want to 2 give the answer, but my question was, was that 3 considered? 4 A. The reason I'm answering it that 5 way, that if you didn't do that, you couldn't 6 do the assay. 7 Q. Was there a question about 8 whether to use a CPE or a PRN as part of the 9 neutralization? 10 A. I'm sorry. The reason I didn't 11 answer the question was you weren't clear in 12 that question. So it's -- but now I 13 understand what you're asking. Not that I 14 recollect. 15 Q. Now, what assay did CBER want, 16 if you recollect? 17 MS. DYKSTRA: Objection to form. 18 THE WITNESS: I do not recollect 19 those direct discussions with CBER. 20 BY MR. BEGLEITER: 21 Q. Did they want -- was it Merck's 22 and your preference to use the ELISA assay? 23 MS. DYKSTRA: Objection to form. 24 THE WITNESS: There was a 25 reference to use the ELISA -- if there</p>	<p style="text-align: right;">Page 89</p> <p>1 withdrawn. 2 Do you have an understanding 3 that CBER wanted a PRN assay to be conducted 4 for this end expiry study? 5 A. Well, CBER agreed to the running 6 of the PRN assay. So, therefore, I assume that 7 they were comfortable with that decision which 8 was made in collaboration with CBER. 9 Q. Well, did Merck agree with CBER 10 when it first suggested a PRN assay? 11 A. No, I don't recollect the details 12 of those initial conversations. 13 Q. Now, were you aware -- well, 14 now, did CBER want a 95 percent -- I'm sorry 15 if this is similar to the question I asked 16 before, but did CBER want a 95 percent 17 seroprotection rate against the wild type 18 isolates? 19 A. I don't recall if CBER 20 specifically wanted that number. 21 Q. And you don't recall whether or 22 not -- or do you recall whether or not CPE was 23 considered as one of the assays? 24 A. CPE is not an assay, so I don't 25 know the question that you're asking.</p>

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<p style="text-align: right;">Page 90</p> <p>1 MR. BEGLEITER: I'm showing the 2 witness -- 3 - - - 4 (Exhibit Emini-3, 9/9/99 Memo, 5 00015686 - 00015689, was marked for 6 identification.) 7 - - - 8 THE WITNESS: CPE refers to 9 cytopathic effect. It's not an assay. 10 MR. BEGLEITER: I'm showing 11 Dr. Emini Merck 00015686 to 89. 12 THE WITNESS: So what this 13 refers to, it refers to an assay that 14 is based upon virus elicited cytopathic 15 effect, or CPE. But what I cannot tell 16 from reading this document was they are 17 the exact parameters nor the design of 18 the assay itself. 19 BY MR. BEGLEITER: 20 Q. On page 2, I think you 21 anticipated me, there's a committee that's 22 established to "bring recommendation of which 23 mumps neutralization assay (CPE or PR) should 24 be used for future studies to the CAS in 25 September '99." [As read] Right?</p>	<p style="text-align: right;">Page 92</p> <p>1 95 percent, per CBER's expectation." [As 2 read] 3 Does this refresh your 4 recollection that CBER had an expectation that 5 there would be a 95 percent seroprotection 6 rate against wild type virus? 7 A. Well, I will take it in terms of 8 what it says here, that CBER did have an 9 expectation that it would be able to 10 demonstrate a 95 percent seroconversion. This 11 is an inappropriate use of the word 12 "seroprotection." It's not the terminology 13 that should be used. 14 Q. In looking at this document, 15 does this refresh your recollection that you 16 were a member of the CAS, the Clinical -- 17 A. No, according to this document, 18 I brought a recommendation to the CAS. I 19 don't recall, as I said earlier, that I was a 20 member of the CAS. 21 Q. Do you know what the -- do you 22 have any recollection of what the independent 23 assays were that confirmed that the 24 seroprotection rates against wild type 25 isolates were not about 95 percent?</p>
<p style="text-align: right;">Page 91</p> <p>1 A. Yeah. 2 Q. This was a committee in which 3 you were the senior member? 4 A. Well, it's -- I don't recall -- 5 I don't recall my exact membership on the 6 committee back in '99. 7 Q. Are you saying that this is a 8 mistake? 9 A. No, no, no. This says to bring 10 the recommendation of the assay to the CAS. I 11 don't remember if I was a member of the 12 committee of the CAS, but I probably did bring 13 the recommendation to the CAS. 14 Q. Among the four people that are 15 listed, you, B. Buckland, Pete Kniskern and A. 16 Shaw, you were the senior person? 17 A. Yes, I was the senior person. 18 Q. Do you recall whether or not 19 a -- was a recommendation brought? 20 A. I do not recall. 21 Q. Go to the first page of this 22 document. "DECISIONS" at the bottom. And it 23 says, "At this point 2 independent assays have 24 confirmed that the seroprotection rates 25 against wild type virus isolates are not about</p>	<p style="text-align: right;">Page 93</p> <p>1 A. I don't recall other than what 2 it says on this document. 3 Q. You can put that away. 4 MS. DYKSTRA: Are you through 5 with Exhibit 3? 6 MR. BEGLEITER: Yes, we're done 7 with it. 8 BY MR. BEGLEITER: 9 Q. Now, there came a time when a 10 decision was made for the PRN assay to be 11 conducted and the lab chosen was Dr. Krah's. 12 Is that right? 13 MS. DYKSTRA: Objection. 14 THE WITNESS: Please repeat the 15 question. 16 BY MR. BEGLEITER: 17 Q. Okay. There came a time when a 18 decision was made to do a PRN assay. Is that 19 correct? 20 A. Yes. 21 Q. And that was assigned to 22 Dr. Krah, Dr. Krah's lab? 23 A. His assignment originally, 24 again, based on documents that I reviewed, was 25 to originally develop the assay.</p>

24 (Pages 90 - 93)

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1 Q. And had he developed any other
 2 PRN assays, to your recollection?
 3 A. It was certainly within his
 4 level of expertise to have done that. I don't
 5 recall which specific assays he may have
 6 developed prior to this time.
 7 Q. Do you know if he developed the
 8 assay for the head-to-head Priorix versus MMR
 9 II assay?
 10 A. I do not recall.
 11 Q. Now, sir, do you know when Merck
 12 started to develop the end expiry trial, about
 13 what year?
 14 A. I don't recall directly. Again,
 15 on the basis of documents that I reviewed
 16 recently, the question came up with regards to
 17 whether or not 4.3 should reflect the end
 18 expiry value, so that would be roughly around
 19 the time that the consideration for it
 20 properly came up, so that would be in 1999,
 21 2000, something along on those lines.
 22 Q. In 1999, was there a --
 23 withdrawn.
 24 Do you know what the word
 25 "overflow" means as related to the mumps

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1 vaccine?
 2 A. It's a standard terminology
 3 within the industry. So what overflow means
 4 is to add more into the unit, whether it be a
 5 vial, a syringe, whatever the case happens to
 6 be, tied more into the unit than what would
 7 normally be required.
 8 Q. And was an overflow performed in
 9 1999?
 10 MS. DYKSTRA: Objection to the
 11 form.
 12 THE WITNESS: I don't recall the
 13 details.
 14 BY MR. BEGLEITER:
 15 Q. I'd like to hand you -- well, do
 16 you recall that an overflow occurred with
 17 regard to the mumps vaccine while you were in
 18 charge of biologics?
 19 A. I don't recall the actual
 20 details, but I do recall, again, on the basis
 21 of documents that I reviewed, was that the
 22 decision was made to fill, not necessarily to
 23 overflow, so I'm being careful with the
 24 terminology here, to fill at a level of five
 25 logs.

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1 Q. And what -- what would that
 2 equal in terms of the TCID50?
 3 A. That would be 100,000.
 4 Q. So that would increase from --
 5 A. 20,000 to 100,000.
 6 Q. Tell me, sir, were you involved
 7 with that decision at all?
 8 A. I was not involved with that
 9 decision.
 10 Q. Do you know who made the --
 11 A. Not that I recollect, of course.
 12 Q. Do you know who was involved?
 13 A. I do not know who was involved,
 14 no.
 15 Q. Did the filling to five log
 16 raise any safety concerns in you?
 17 A. They did not at the time. I
 18 don't remember what my thoughts were obviously
 19 you know, 20 years ago, but I would not have
 20 raised any safety concerns then and don't
 21 raise any safety concerns now. Again, the
 22 decision was most likely than not taken with
 23 the concurrence of the agency.
 24 Q. The amount of vaccine here goes
 25 from 20,000 to 50,000, it quintuples. Right?

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1 A. 20,000 to 100,000.
 2 Q. 20,000, I'm sorry, to 100,000,
 3 quintuples. Do you know whether it raised any
 4 concerns or not of you that to you whether or
 5 not any safety tests were taken, field or
 6 clinical?
 7 A. No. I presume that there --
 8 well, it -- there were -- one would need to go
 9 back and take a look at the original studies
 10 that were done when the vaccine was first
 11 licensed. And somewhere in those studies
 12 there's an indication of the levels of virus
 13 that were -- of vaccine virus that were tested
 14 in children at the time for safety purposes.
 15 But I don't know what those were.
 16 Q. During your tenure at biologics,
 17 at the division, was there any consideration
 18 to increasing the fill again, that you recall?
 19 MS. DYKSTRA: Objection.
 20 THE WITNESS: I was only aware
 21 of this one.
 22 BY MR. BEGLEITER:
 23 Q. I didn't say it happened, was
 24 there a consideration of doing it, of filling
 25 in more?

25 (Pages 94 - 97)

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<p style="text-align: right;">Page 98</p> <p>1 A. I don't understand your question. 2 Q. Was there consideration of 3 increasing the amount of virus by more than 4 five log? 5 A. Not to my knowledge. 6 MS. DYKSTRA: I think the court 7 reporter got something incorrect on the 8 transcript. Do you mind if I just read 9 it to make sure? 10 MR. BEGLEITER: Sure, go ahead. 11 MS. DYKSTRA: You asked him if 12 the fill to five log raised any safety 13 concerns and you said they did not at 14 the time. I don't remember what my 15 thoughts were obviously, you know, 16 20 years ago. Again, the decision was 17 most likely not taken with the 18 concurrence of the agency or taken 19 with? 20 THE WITNESS: No, taken with the 21 concurrence of the agency. 22 MR. BEGLEITER: Okay. That's 23 fine. That's fair. That's how I heard 24 it. 25 MS. DYKSTRA: Thank you. Just</p>	<p style="text-align: right;">Page 100</p> <p>1 Q. And you would have received it 2 in the usual course of your employment with 3 Merck? 4 A. I would have received it in the 5 usual course of my employment, of course. 6 Q. You can put it aside. I'm not 7 going to ask you any substantive questions 8 about it. 9 So what's a warning letter from 10 CBER? 11 A. It's exactly what it says. It's 12 a warning letter from CBER in which the agency 13 indicates specific deficiencies that it wishes 14 to see corrected immediately. And it gives 15 the recipient a relatively short period of 16 time to put together a correction plan that 17 the agency would then need to certify. 18 Q. And what could happen if CBER is 19 not satisfied with the correction plan? 20 A. Again, it depends on what's the 21 nature of the warning letter. If the warning 22 letter reflects a manufacturing facility, they 23 will close down a manufacturing facility. If 24 it refers to a specific product, they can 25 request withdraw of the product. It depends</p>
<p style="text-align: right;">Page 99</p> <p>1 wanted to make sure it was clear. 2 Thanks. 3 BY MR. BEGLEITER: 4 Q. Sir, I'd like to show you a 5 document with Bates number 00615147 through 6 174. I'm going to show it to you, but I'm 7 telling you, I'm not going to ask you any 8 questions about the substance of it. This is 9 what's called the authentication process. I'm 10 going to ask you whether or not you received 11 it. Okay? There will be several documents 12 like this. 13 - - - 14 (Exhibit Emini-4, 10/2/02 E-mail 15 with attachment, 00615147 - 00615174, 16 was marked for identification.) 17 - - - 18 BY MR. BEGLEITER: 19 Q. All I'm going to ask you is 20 whether or not you received this document in 21 the course of your -- 22 A. I have no direct recollection of 23 having received this specific document, but 24 given that it was addressed to me, I will 25 assume that I received it.</p>	<p style="text-align: right;">Page 101</p> <p>1 on the details. 2 - - - 3 (Exhibit Emini-5, 2/9/01 Warning 4 letter, was marked for identification.) 5 - - - 6 BY MR. BEGLEITER: 7 Q. Sir, again, I'm going to ask you 8 a question, have you ever seen this document 9 before? 10 A. Allow me a few minutes, please. 11 Q. Sure. 12 A. Again, I don't recall specifically 13 having received this document, and there is no 14 indication here that this was in any way 15 addressed to me, so I don't know. 16 Q. But considering your position, 17 would this have been something that would have 18 been sent? 19 A. No, not necessarily. This was a 20 note that was sent to Dr. Roberta McKee, vice 21 president of vaccine and sterile quality 22 operations. This would have been the Merck 23 manufacturing division which is a completely 24 separate decision of the corporation from the 25 Merck Research Laboratories.</p>

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1 Q. Put it aside, sir.
 2 Sir, do you know what a
 3 validation protocol is?
 4 A. Yes, sir.
 5 Q. What's a validation protocol?
 6 A. A validation protocol is, again,
 7 it depends what the context is in which one is
 8 using the terminology, but for an assay, let's
 9 put it that way, for an assay validation
 10 protocol is a protocol that one conducts to
 11 validate the operational parameters of the
 12 assay, the variability of the assay, the
 13 variance of the assay, the reproducibility of
 14 the assay, a statistical determination of how
 15 one actually interprets the quantitative
 16 values that the assay generates. It's a
 17 statistically run and statistically predefined
 18 protocol that once those parameters are
 19 established for the assay, then essentially
 20 validates the assay. It's an old terminology.
 21 Terminology has changed since then. It's now
 22 referred to as assay qualification.
 23 Q. Were there validation assays for
 24 Protocol 007?
 25 MS. DYKSTRA: Objection. Form.

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1 THE WITNESS: So, again, based
 2 upon my review, as would have been the
 3 case for any assay in support of a
 4 clinical study, the assay would have
 5 been validated, yes.
 6 BY MR. BEGLEITER:
 7 Q. Would it have been at least one
 8 for ELISA and one for the PRN assay?
 9 A. Yes, we would do separate
 10 validations for each assay.
 11 Q. What is vaccine biometrics
 12 research, what division of that -- is that?
 13 A. That was a statistical group in
 14 support of vaccine research, vaccine clinical
 15 studies.
 16 Q. Would you have reviewed -- or
 17 did you review any of the validation protocols
 18 for Protocol 007?
 19 A. I have no direct recollection,
 20 but it is unlikely I would have reviewed the
 21 validation protocols. I would have relied on
 22 the, in fact, statistical group to determine
 23 whether or not an appropriate validation had
 24 been conducted. Validation is a statistical
 25 operation.

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1 Q. Did you sign off on any
 2 validations --
 3 A. Not that I recall.
 4 Q. Would you recognize what a
 5 validation looks like for 007?
 6 A. Probably so.
 7 Q. I'm going to show you a fairly
 8 thick document but one that I'm only going to
 9 ask you to look at a few pages. It bears
 10 Merck number MRK-KRA0017036 to 114. Give it
 11 to the court reporter and give it to you.
 12 MS. DYKSTRA: Exhibit 6.
 13 - - -
 14 (Exhibit Emini-6, FDA Response
 15 to MMR II, 00017036 - 00017115, was
 16 marked for identification.)
 17 - - -
 18 BY MR. BEGLEITER:
 19 Q. Go to the third page which has
 20 contained 17038. Have you seen this letter
 21 before?
 22 A. Not to my recollection.
 23 Q. Do you know what AIGENT stands
 24 for, A-I-G-E-N-T?
 25 A. I cannot -- again, I can't tell

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1 you what the exact terminology stands for,
 2 but, again, on the basis of documents that I
 3 recently reviewed, it was in reference to the
 4 actual plaque reduction neutralization assay
 5 that was being used in clinical evaluation of
 6 007.
 7 Q. We've already discussed the
 8 study entitled -- I guess, rather the study
 9 titled, "A Study of MMR II at Mumps Expiry
 10 Potency in Healthy Children 12 to 18 Months of
 11 Age"?
 12 A. Then it would be 007.
 13 Q. Fine. This letter says that
 14 there's a summary of validation, and among
 15 other things, but all I'm going to ask you,
 16 sir, is to turn to page 17080. Actually turn
 17 first to 17076. You can look at it in
 18 combination if you wish with the next document
 19 beginning at 080 going to the end.
 20 All I'm going to ask you, sir --
 21 I'm not going to ask you for any questions
 22 about the substance of this document. I'm
 23 going to ask you whether or not this appears
 24 to you to be the validation protocol for
 25 Protocol 007 as it relates to PRN, the plaque

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<p style="text-align: right;">Page 106</p> <p>1 reduction neutralization? 2 A. Well, give me a second. 3 Q. Take a second. 4 MS. DYKSTRA: Take time if you 5 need to look at the cover letter as 6 well. I'm not directing you to look at 7 anything, but take time to look at 8 whatever time you need to make sure 9 you're comfortable. 10 THE WITNESS: Yes, this does 11 appear to be the validation protocol 12 and the validation results for the 13 assay. 14 BY MR. BEGLEITER: 15 Q. Going to the first page, this 16 appears to have been sent to CBER on March 12, 17 2001. 18 A. On the cover page it is 19 March 12, 2001, yes. 20 Q. Again, you don't recollect 21 whether you actually reviewed this before 22 you -- before it went to CBER? 23 A. Not my recollection, no. 24 Q. You don't recall whether you 25 signed off on it?</p>	<p style="text-align: right;">Page 108</p> <p>1 me, yes. 2 Q. Do you recall seeing this 3 document? 4 A. Again, subsequent to reviews of 5 documents over the last period of time, I do 6 recall receiving this document, the first page 7 which is the actual 483 document itself. 8 Q. You saved me a question. A 483, 9 to be clear, is the sort of notice of 10 deficiency that -- 11 A. 483 is a notice of inspection 12 observations that the inspector wishes to 13 bring to your attention. 14 Q. And there was -- according to 15 the second page which you said you recall, the 16 inspection occurred on what day? 17 A. The inspection occurred on 18 8/6/01, August 6, 2001. 19 Q. This e-mail was sent to you by 20 Karen McKenney on August 7th, the next day? 21 A. Well, the memorandum is dated 22 August 6th. The e-mail is dated August 7th, 23 yes. 24 Q. And sir, I just want to you to 25 take a look at number 1.</p>
<p style="text-align: right;">Page 107</p> <p>1 A. I don't recall. It's timed. I 2 don't recall. 3 Q. Okay. Fine. 4 MR. BEGLEITER: I'm going to 5 hand the court reporter Merck 00052249 6 through 53, ask her to mark it. What's 7 the number on this? 8 COURT REPORTER: 7. 9 THE WITNESS: 7. 10 MR. BEGLEITER: Okay. Emini-7. 11 - - - 12 (Exhibit Emini-7, 8/7/01 E-mail 13 with attachment, 00052249 - 00052253, 14 was marked for identification.) 15 - - - 16 BY MR. BEGLEITER: 17 Q. You are permitted to look at the 18 whole thing, but I'm only going to be asking 19 you questions about the cover e-mail and 20 what's behind the cover e-mail, 483. 21 A. Okay. 22 Q. Now, the first question is, sir, 23 did you receive this document in the usual 24 course of your employment? 25 A. Yes, I did. It's addressed to</p>	<p style="text-align: right;">Page 109</p> <p>1 MS. DYKSTRA: On the 483? 2 THE WITNESS: On the 483? 3 BY MR. BEGLEITER: 4 Q. I'll read it to you. Number 1 5 says, "Raw data is being changed with no 6 justification, for example...," and then it 7 gives a series of numbers which I'm not going 8 to read to you. Do you have an understanding 9 sitting here today of what that meant, what 10 that referred to? 11 A. What that referred to was, 12 again, remember 483 is a notice of 13 observations that the agency or that the 14 inspector specifically actually in the end 15 wishes to have some explanation for. So if 16 the inspector was not able to find at the time 17 that she conducted this inspection was that 18 there were changes being made to the data 19 related to whatever assay she was looking at, 20 that did not have clear justification noted 21 when the changes were made. 22 Q. And do you know Mr. Krahling who 23 was sitting here -- 24 A. Yes, I did. 25 Q. -- sitting at this table? Did</p>

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<p style="text-align: right;">Page 110</p> <p>1 he warn you of this before August 7, 2001?</p> <p>2 MS. DYKSTRA: Objection. Form.</p> <p>3 THE WITNESS: I have no</p> <p>4 recollection of any discussions with</p> <p>5 Mr. Krahlung related to this issue save</p> <p>6 one. Again, this was as a result of</p> <p>7 review of documents, and the document</p> <p>8 that I saw that indicated that at some</p> <p>9 point, and I don't remember what the</p> <p>10 date is, Mr. Krahlung came to me to</p> <p>11 show me -- to express his concerns and</p> <p>12 presumably show me some data on which</p> <p>13 he had his concerns.</p> <p>14 BY MR. BEGLEITER:</p> <p>15 Q. And was that concern that data</p> <p>16 was being changed with no justification?</p> <p>17 A. I don't recall the nature of</p> <p>18 that concern.</p> <p>19 Q. You can put this away.</p> <p>20 Well, I'll ask you, did you work</p> <p>21 on a response to 483? Did you review a</p> <p>22 response to the 483?</p> <p>23 A. Yes, I reviewed. Again, no</p> <p>24 direct recollection, but, again, based on</p> <p>25 review of documents, I was involved in</p>	<p style="text-align: right;">Page 112</p> <p>1 A. I signed that letter.</p> <p>2 Q. Your signature?</p> <p>3 A. That is my signature.</p> <p>4 Q. And, again, you can put this</p> <p>5 away, I have some questions to ask. I'm not</p> <p>6 going to ask any questions about that</p> <p>7 document, at least right now.</p> <p>8 Well, the purpose of this</p> <p>9 document was -- the purpose of this document,</p> <p>10 was it to respond the 483 of August 6, 2001?</p> <p>11 A. Right. The 483 was August 6th,</p> <p>12 the response went back on August 20th.</p> <p>13 Q. And tell me, sir, what did you</p> <p>14 do between August 6th and August 20th that</p> <p>15 compiled information for you to respond to the</p> <p>16 483?</p> <p>17 A. Well, again, I have no direct</p> <p>18 recollection because of the period of time.</p> <p>19 MS. DYKSTRA: I just caution you</p> <p>20 not to disclose any communications with</p> <p>21 counsel related to the response or</p> <p>22 anything you did to generate the</p> <p>23 response, but otherwise, you can</p> <p>24 respond.</p> <p>25 THE WITNESS: Yes. No, that's</p>
<p style="text-align: right;">Page 111</p> <p>1 responding to the 483 and reviewing the</p> <p>2 responses to the 483, yes.</p> <p>3 MR. BEGLEITER: I'll have the</p> <p>4 court reporter, please, mark this. I</p> <p>5 guess we're now up to 8, Emini-8. It's</p> <p>6 a document bearing Bates numbers Merck</p> <p>7 481 to 539. I'd like the witness to</p> <p>8 look at it. It's being circulated to</p> <p>9 other counsel.</p> <p>10 - - -</p> <p>11 (Exhibit Emini-8, 8/20/01 Letter</p> <p>12 with attachment, 00481 - 00539, was</p> <p>13 marked for identification.)</p> <p>14 - - -</p> <p>15 BY MR. BEGLEITER:</p> <p>16 Q. Okay. And, sir, do you recognize</p> <p>17 this document?</p> <p>18 A. Yes. This would have been the</p> <p>19 formal response to the FDA to the four</p> <p>20 observations listed on the 483.</p> <p>21 Q. And on page -- on the cover --</p> <p>22 on the first sheet there's a letter. Is that</p> <p>23 right?</p> <p>24 A. That is correct.</p> <p>25 Q. Who signs that letter?</p>	<p style="text-align: right;">Page 113</p> <p>1 fine. So the -- thank you very much.</p> <p>2 No, so the -- what I did is reflected</p> <p>3 right here in the responses. Worked</p> <p>4 with the team to pull together the</p> <p>5 responses that needed to be done.</p> <p>6 BY MR. BEGLEITER:</p> <p>7 Q. So did you commence any kind of</p> <p>8 investigation of what happened?</p> <p>9 A. Of course.</p> <p>10 MS. DYKSTRA: Objection to the</p> <p>11 extent that that involves counsel. You</p> <p>12 can answer yes and no and you can</p> <p>13 discuss any other investigation.</p> <p>14 BY MR. BEGLEITER:</p> <p>15 Q. Let me just -- I'll put a point</p> <p>16 on this. I'm not going to ask you any</p> <p>17 questions about what you may have said to</p> <p>18 counsel or counsel to said to you. Okay?</p> <p>19 A. Fair enough.</p> <p>20 Q. However, let me ask you the</p> <p>21 question, did you consult with counsel after</p> <p>22 the 483 was received by you?</p> <p>23 A. I consulted with counsel, but,</p> <p>24 again, based upon the review of documents,</p> <p>25 again, of which were recently -- I recently</p>

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<p style="text-align: right;">Page 114</p> <p>1 reviewed, I consulted with counsel immediately</p> <p>2 prior actually to the receipt of the 483. And</p> <p>3 consultation with counsel was in the context</p> <p>4 of --</p> <p>5 MS. DYKSTRA: Just to caution</p> <p>6 you not to disclose the content of --</p> <p>7 MR. BEGLEITER: Let him answer</p> <p>8 the question.</p> <p>9 MS. DYKSTRA: You can say the</p> <p>10 time and the date, if you recall.</p> <p>11 MR. BEGLEITER: Let him answer</p> <p>12 the question.</p> <p>13 THE WITNESS: What I do recall</p> <p>14 was --</p> <p>15 MS. DYKSTRA: Appropriately --</p> <p>16 MR. BEGLEITER: I'm not asking</p> <p>17 for any attorney-client communication.</p> <p>18 MS. DYKSTRA: He cannot disclose</p> <p>19 any communications.</p> <p>20 BY MR. BEGLEITER:</p> <p>21 Q. I'm not asking for any communication</p> <p>22 between you. I asked you whether or not</p> <p>23 you consulted with --</p> <p>24 A. Yes, I consulted with counsel.</p> <p>25 COURT REPORTER: Who am I</p>	<p style="text-align: right;">Page 116</p> <p>1 A. That, I actually do not recollect.</p> <p>2 Q. And do you recollect if counsel</p> <p>3 was involved in drafting the response which</p> <p>4 is -- I think it's Emini-9, the letter?</p> <p>5 A. Emini-8.</p> <p>6 Q. Emini-8.</p> <p>7 A. Emini-8, yes. Normally counsel</p> <p>8 would not have been involved in these</p> <p>9 discussions. These are regulatory discussions.</p> <p>10 But, again, I have no direct recollection.</p> <p>11 Q. As far as you know, everything</p> <p>12 in this document is correct, in Emini-8?</p> <p>13 A. I signed it, yes, I believe it</p> <p>14 is.</p> <p>15 Q. Now, sir, looking at Emini-8,</p> <p>16 was that the final response regarding the 483</p> <p>17 or was there an additional response?</p> <p>18 A. I don't -- regarding the</p> <p>19 observations on the 483, this is the response.</p> <p>20 I do not recall if there were subsequent</p> <p>21 communications. Oftentimes there are. And,</p> <p>22 in fact, I believe there probably are.</p> <p>23 Q. Do you recall any teleconferences</p> <p>24 with CBER regarding your response?</p> <p>25 A. Not an exact recollection of the</p>
<p style="text-align: right;">Page 115</p> <p>1 supposed to take?</p> <p>2 BY MR. BEGLEITER:</p> <p>3 Q. I'm sorry. I'll ask the</p> <p>4 question again.</p> <p>5 Did you consult -- I'll ask it a</p> <p>6 little differently.</p> <p>7 Did you consult with counsel</p> <p>8 after you received the 483?</p> <p>9 A. I do not recollect that I</p> <p>10 consulted with counsel after I received the</p> <p>11 483. Again, based on the review of documents,</p> <p>12 I believe that I consulted with counsel</p> <p>13 immediately prior to the receipt of the 483.</p> <p>14 Q. Again, without telling me any</p> <p>15 communication, why did you consult with</p> <p>16 counsel prior to receiving the 483?</p> <p>17 A. Again, based on the review of</p> <p>18 documents, I consulted with counsel</p> <p>19 immediately after I met had with Mr. Krahling,</p> <p>20 and Mr. Krahling brought his concerns to my</p> <p>21 attention.</p> <p>22 Q. I see. So you remember that,</p> <p>23 but you don't remember whether or not you</p> <p>24 consulted with counsel after you received the</p> <p>25 483?</p>	<p style="text-align: right;">Page 117</p> <p>1 teleconferences, per se, but, again, on the</p> <p>2 basis of review of documents, there were</p> <p>3 teleconferences with CBER subsequent to this.</p> <p>4 Q. You don't recollect anything</p> <p>5 regarding the substance of those teleconferences?</p> <p>6 A. Only on the basis of what I</p> <p>7 reviewed.</p> <p>8 Q. Well, what --</p> <p>9 A. So on the basis of -- again, my</p> <p>10 recollection, only on the basis of what I</p> <p>11 recently reviewed, those were clarified -- I</p> <p>12 don't recall the specific details, but they</p> <p>13 reflected clarifying back and forth discussions</p> <p>14 between the agency and the company of the</p> <p>15 basis of the answers and to further clarify</p> <p>16 whatever additional questions that the agency</p> <p>17 might have. It's a pretty standard practice.</p> <p>18 Q. Do you recall who you spoke with</p> <p>19 at the agency?</p> <p>20 A. I don't recall even if I was</p> <p>21 present for that. The conversation would have</p> <p>22 been held between our regulatory liaison and</p> <p>23 the agency.</p> <p>24 Q. Do you know a woman named Cathy</p> <p>25 Carbone, Dr. Cathy Carbone?</p>

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<p style="text-align: right;">Page 118</p> <p>1 A. I know who she is. I don't 2 recall if I spoke with her. 3 Q. Just eliminated a document. 4 Sir, going back a little bit in 5 time, sorry to be out of chronological order, 6 do you recall, again, about when, what year 7 and when, what season the overfilling took 8 place for the mumps vaccine? 9 A. No, I don't. 10 Q. Do you recall Merck being 11 requested by CBER to give the seroconversion 12 rates that it was getting on Protocol 007 to 13 CBER sometime in 1999? 14 MS. DYKSTRA: Objection. Form. 15 THE WITNESS: I don't understand 16 the question. Sorry. Please, one more 17 time? 18 BY MR. BEGLEITER: 19 Q. CBER would from time to time ask 20 you some results of some clinical trials, 21 testing, whatever. Right? 22 MS. DYKSTRA: Objection to the 23 form. 24 BY MR. BEGLEITER: 25 Q. Isn't that true, in your</p>	<p style="text-align: right;">Page 120</p> <p>1 necessarily in terms of direct reporting 2 relationship, but she had overall coordinating 3 responsibilities. We'll go with that. 4 Q. And while you were in biologics, 5 did you work with her? 6 A. Yes, I did. 7 Q. Did you work with Dr. Scolnick? 8 A. Well, Dr. Scolnick was the 9 president of the research laboratories. 10 Q. Well, I'm saying you actually 11 did things with him, discussed things with 12 him? 13 A. Mostly in formal settings, yes. 14 Q. I'm sorry, informal or formal? 15 A. Mostly in formal settings. 16 MR. BEGLEITER: I'd like to show 17 you Merck 1898768 through 72. 18 - - - 19 (Exhibit Emini-9, 10/31/99 20 E-mail with attachment, 01898768 - 21 01898772, was marked for identification.) 22 - - - 23 BY MR. BEGLEITER: 24 Q. We're calling it Emini-9. 25 A. Okay.</p>
<p style="text-align: right;">Page 119</p> <p>1 experience? 2 A. It depends on the nature of 3 what's being discussed and what it is. I 4 mean, typically CBER would wait until the end 5 of a study before asking for any data from a 6 study. 7 Q. Do you recall with regard to 8 Protocol 007, did they ask before the study? 9 A. I don't recall. 10 Q. Now, what relationship, what 11 position did Mr. -- Dr. Scolnick have in the 12 time that you were at the biologics? 13 A. He was the president of the 14 research laboratories. 15 Q. He was -- at least in terms of a 16 pecking order, he was above you? 17 A. We went through this already 18 with Ford-Hutchinson. Yes. 19 Q. Fine. Who is Dr. Dorothy 20 Margolskee? 21 A. So Dr. Margolskee was in the 22 research laboratories. She had a general 23 responsibility over vaccine-related medical 24 and research questions, predominantly medical 25 and regulatory questions. So she had, not</p>	<p style="text-align: right;">Page 121</p> <p>1 Q. Turning to page 69, 769, the 2 bottom bullet point, "Mumps neutralizing 3 antibody assay." Second sentence, "Prior to 4 discussing the unanticipated low SCR for mumps 5 with CBER, the results from sera from the 6 head-to-head trial from MMR II and Priorix 7 will be reviewed to confirm that this low SCR 8 is observed in both products." 9 Do you see that? 10 A. Yes. 11 Q. Questions on this. First of 12 all, do you have a recollection about whether 13 there was an unanticipated low seroconversion 14 rate for mumps on the MMR II product? 15 MS. DYKSTRA: Objection. Form. 16 THE WITNESS: So the discussion 17 around this revolved around whether or 18 not the assay -- now, remember, the 19 assay was being redeveloped because the 20 original assay that was used when the 21 vaccine was first licensed no longer 22 existed. The indicator strains didn't 23 exist anymore, no one even knew what 24 they were. So they didn't exist. 25 So going back to our previous</p>

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<p style="text-align: right;">Page 122</p> <p>1 discussion, the note was, from CBER, 2 that this was -- presumably from CBER, 3 certainly in agreement with CBER, that 4 the seroconversion rate needed to be 5 assessed in a plaque reduction 6 neutralization assay or a CPE-based 7 assay, either way, with a wild type 8 strain yielding, all right, yielding a 9 level of seroconversion that was 10 approximately 90 percent as noted in 11 the first sentence because of the need 12 for sensitivity in the assay and 13 reflecting the known field efficacy of 14 the vaccine. What was occurring 15 apparently was that -- not apparently 16 but for a fact, again, based upon 17 what's here, and I do recall this, what 18 was known, what was observed was that 19 with different wild type strains -- or 20 wild type isolates, rather, of the 21 virus, seroconversion rates were 22 notably lower than 90 percent and, 23 therefore, the assay was not giving a 24 set of results that was reflective of 25 the vaccine's known efficacy, and,</p>	<p style="text-align: right;">Page 124</p> <p>1 A. That is correct. 2 Q. Again, the sentence I read to 3 you, why wait for the results of the 4 head-to-head MMR II and Priorix before telling 5 CBER what the results -- the SCR results were? 6 MS. DYKSTRA: Objection. Form. 7 THE WITNESS: The only reason 8 for doing that was to be able to 9 essentially have an independent 10 verification that the primary driver 11 for the lower seroconversion that was 12 being observed, okay, was a function of 13 the assay itself. In other words, if 14 you got two independent vaccines, both 15 of which elicit lower seroconversion 16 rates as measured using the Lo1 virus, 17 one can -- and knowing that the field 18 efficacy data pretty much supports, 19 does for a fact support that both 20 vaccines are effective, then -- because 21 both are licensed vaccines in various 22 parts of the world, then one can 23 conclude that the assay that was being 24 developed using the Lo1 virus, was not 25 fit for purpose for the intended reason</p>
<p style="text-align: right;">Page 123</p> <p>1 therefore, could not be used for the 2 kind of comparison we were discussing 3 needed for the 007 study. 4 BY MR. BEGLEITER: 5 Q. Known efficacy referring to what 6 was happening in the field? 7 A. Recurrent efficacy can only be 8 determined in the field. 9 Q. Just straightening that out. 10 In the first sentence where it 11 says, "...with JL as the test isolate....," is 12 that Jeryl Lynn? 13 A. I presume it is Jeryl Lynn, yes. 14 Q. And using the clinical -- in the 15 clinical testing, there was the seroconversion 16 rates -- 17 A. Was approximately 90 percent. 18 Q. And also but for Lo1, do you 19 know what Lo1 stands for? 20 A. Lo1 probably is the designation 21 for another wild type virus test isolate. 22 Q. You don't remember what that is? 23 A. I don't remember exactly what it 24 is, but I'm sure that's what it is. 25 Q. That was 70 to 75 percent?</p>	<p style="text-align: right;">Page 125</p> <p>1 for the vaccine -- the assay was being 2 developed for the 007 study. 3 BY MR. BEGLEITER: 4 Q. So what you're saying here is 5 that because of the unanticipated low SCR for 6 MMR II, you wanted to have or Merck wanted to 7 have the results for the head-to-head to 8 buttress what it was doing? 9 MS. DYKSTRA: Objection. 10 BY MR. BEGLEITER: 11 Q. To buttress the results? 12 A. That's not what I said. What I 13 said was by having the data from sera from 14 children that had received an independent 15 licensed and, therefore, efficacious vaccine, 16 because remember -- I'm going to take a step 17 back. The purpose for developing the assay 18 was to develop an assay that would measure an 19 immunological response elicited by the vaccine 20 that would correlate with the known, the known 21 established efficacy of the vaccine. 22 So here we have an assay using 23 the Lo1 virus that was given a seroconversion 24 rate of 70 percent, yet we know the vaccine is 25 much more effective than what would be</p>

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<p style="text-align: right;">Page 126</p> <p>1 reflected by that level. That would tend to 2 suggest that there is something not, 3 quote/unquote, correct about the assay in 4 terms of what it was reflecting that the 5 vaccine was actually doing. By having data 6 from two -- from sera from children who 7 received independently two known efficacious 8 vaccines, the fact that both vaccines elicited 9 immune responses that gave rise to a result 10 that was roughly around 70 percent using the 11 Lo1 virus, allows you to firmly conclude that 12 and assay developed using the Lo1 virus is not 13 fit for purpose and that it is incapable of 14 giving you the kind of sensitivity that is 15 required to answer the question that was being 16 posed by the 007 trial. 17 Q. If -- I believe you're saying 18 that the efficacy in the field answers the 19 question as to the efficacy of the -- 20 A. It is the only way to address 21 efficacy. 22 MS. DYKSTRA: Object to the 23 form. 24 BY MR. BEGLEITER: 25 Q. And why have --</p>	<p style="text-align: right;">Page 128</p> <p>1 Q. Let me ask it a different way. 2 A. Let's be precise. 3 Q. Let's ask it a different way. 4 The test was being conducted to 5 see what the potency was at expiry. Isn't 6 that right? 7 MS. DYKSTRA: Objection. Form. 8 THE WITNESS: The test was being 9 conducted, which test, the study or the 10 clinical study? 11 BY MR. BEGLEITER: 12 Q. 007. 13 A. The clinical study was being 14 conducted to generate data that would support 15 a vaccine potency level for mumps at the end 16 of shelf life; so, therefore, the expiry 17 potency level. 18 Q. But the conclusion you already 19 had was that since it was efficacious in the 20 field, that no matter what that number was, it 21 was -- the vaccine was fit for purpose. Isn't 22 that what you're saying? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: The conclusion was 25 that the vaccine that was being used</p>
<p style="text-align: right;">Page 127</p> <p>1 MS. DYKSTRA: I objected to the 2 form of the question. 3 BY MR. BEGLEITER: 4 Q. Then if your conclusion is 5 because of what's happening in the field that 6 the mumps virus is fit for purpose -- 7 A. The vaccine. 8 Q. Excuse me, the mumps vaccine is 9 fit for purpose as it stood, then why have 10 Protocol 007 at all? 11 A. The purpose for Protocol 007 was 12 to provide the data that would allow both the 13 company and the agency to define an end expiry 14 number that it could then place in the label. 15 Q. And if that clinical study were 16 to show a -- 17 A. End expiry potency number. 18 Q. If that clinical study was to 19 show that the potency had fallen below 90 20 percent, wouldn't that be something of 21 interest to the CBER? 22 MS. DYKSTRA: Objection. Form. 23 THE WITNESS: Repeat your 24 question because you're mixing words. 25 BY MR. BEGLEITER:</p>	<p style="text-align: right;">Page 129</p> <p>1 from the time the vaccine was licensed 2 up until the time that this entire 3 discussion occurred, which was late 4 '90s, early 2000s, that the vaccine 5 that was being used in the field was 6 indeed efficacious. 7 BY MR. BEGLEITER: 8 Q. And this study was designed to 9 show that the vaccine was fit for purpose? 10 A. No. The study was designed to 11 develop a number, to provide data that would 12 support a number, a value for potency that 13 could be placed in the label for determination 14 of end expiry potency at the end of shelf 15 life. 16 Q. And why was end expiry potency 17 important to CBER? 18 A. It was important for control 19 purposes. And what I mean by control purposes 20 is so that there is a consistency and you can 21 determine a consistency at which point -- in 22 terms of shelf life. So if over time, if a 23 particular batch of vaccine were to lose 24 potency for whatever reason and were to drop 25 below a given level, a given number which was</p>

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<p style="text-align: right;">Page 130</p> <p>1 your end expiry potency, you could declare 2 that, you know, there was loss of control 3 potentially in the production of the vaccine 4 or in the storage of the vaccine. Doesn't 5 mean that the vaccine is no longer effective. 6 That there was simply loss of control. 7 Q. So the premise for this Protocol 8 007 was that MMR/V, the mumps part of it at 9 least, was effective? 10 A. Yes. 11 MS. DYKSTRA: Objection to the 12 form. 13 BY MR. BEGLEITER: 14 Q. Premise going in? 15 MS. DYKSTRA: MMR/V wasn't in 16 the study. 17 BY MR. BEGLEITER: 18 Q. Excuse me, MMR II. 19 A. MMR II. 20 Q. MMR II. Yes. 21 A. That the mumps component -- 22 we'll stick with the mumps component. That 23 the mumps component in MMR II -- 24 Q. Yes. 25 A. -- was absolutely effective.</p>	<p style="text-align: right;">Page 132</p> <p>1 testing? 2 A. Well, according to this, the 3 assays had been developed, that there was a 4 PRN assay and the CPE assay, apparently both 5 assays were being -- I'm reading what's in the 6 rest of the document, that were being done. 7 And they were being developed, you know, 8 probably with the concurrence, not probably 9 but for a fact, with the concurrence of the 10 agency using a wild type virus. And with a 11 wild type virus, and, again, reading through 12 the rest of the document, one of the ones that 13 was used, probably the initial one that was 14 used was this Lo1 wild type virus. It was 15 giving seroconversion rates that were much 16 lower than 90 percent, approximately 70 percent. 17 And that was not going to meet the agency's 18 requirement for a sensitive enough test that 19 would allow you to answer the questions posed 20 by 007. 21 Q. Do you know if the agency was 22 told, if CBER was told about the low SCR for 23 Lo1? 24 A. Based on documents that I 25 reviewed, these were discussions that were</p>
<p style="text-align: right;">Page 131</p> <p>1 Q. And that's the premise going in? 2 A. That is the observed fact. It's 3 effective. 4 Q. And let's just -- while we're on 5 the subject, let's go to the first paragraph, 6 MMR II end expiry. It says that -- first 7 sentence tells you how many people, how many 8 subjects are enrolled. Skip that. Then it 9 says, "The primary study hypothesis of a..." 10 A. Seroconversion rate. 11 Q. "...seroconversion rate equal to 12 or greater than 90 percent against wild type 13 mumps...is unlikely to be met..." [as read] 14 A. Right. 15 Q. "...and therefore...should be 16 revised either in terms of addressing the 17 hypothesis or addressing the technical 18 limitations of the assays used to date." 19 A. Right. 20 Q. And this is in October 31, 1999. 21 Right? 22 A. Right. 23 Q. Do you know if by then there had 24 even -- that the PRN had actually been set up 25 to do any kind of assay work, any kind of</p>	<p style="text-align: right;">Page 133</p> <p>1 going on in collaboration with the agency 2 because the agency very much wanted an assay 3 that would answer the question that would 4 allow them to establish a value for end expiry 5 in the label. An SCR of 70 percent, all 6 right. So what we know is the following: We 7 know that the vaccine is effective -- 8 Q. My question -- 9 MS. DYKSTRA: Let him answer. 10 MR. BEGLEITER: He's not 11 answering my question. 12 THE WITNESS: I will get into 13 the answer. Allow me to answer the 14 question, please. 15 What we know is that the vaccine 16 is effective, it's been given to 17 children, to all the children in the 18 study, and that the assay that had been 19 developed using Lo1 was only yielding 20 an SCR of 70 percent. That would not 21 have been fit for purpose. That 22 indicates that the assay, the assay is 23 not fit for purpose. It's not allowing 24 you to determine whether or not -- it 25 was not allowing you to -- would not</p>

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1 allow you, it would not prospectively
 2 allow you to determine whether or not
 3 there would be a difference in the
 4 seroconversion rate that would be
 5 statistically acceptable among the
 6 different, the three different potency
 7 levels that were being tested in 007.
 8 So, therefore, the discussion with the
 9 agency was how can we modify the assay
 10 that would give us an assay or assays
 11 of sufficient sensitivity.
 12 MR. BEGLEITER: Can you read the
 13 question back, please.
 14 - - -
 15 (The court reporter read the
 16 pertinent part of the record.)
 17 - - -
 18 BY MR. BEGLEITER:
 19 Q. Do you know if they were told
 20 specifically about what the low SCR was?
 21 A. I do not recall what the
 22 specific conversation was. What I do recall
 23 was that there were ongoing conversations with
 24 the agency to generate an assay with
 25 sufficient sensitivity.

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1 Q. But you don't recall whether or
 2 not somebody said, you know, we've done an
 3 assay on Lo1 and the SCR is 70 to 75 percent?
 4 A. What I do recall -- no, I don't
 5 recall that specific question.
 6 Q. That's my question. Okay.
 7 A. That specific discussion.
 8 Q. Now, in terms of whether CBER
 9 was going to be -- whether CBER was going to
 10 be told about the unanticipated low SCR, back
 11 to the last paragraph on that page, when the
 12 results from the head-to-head trial with
 13 MMR II and Priorix was available. Was that
 14 discussed with Dr. Scolnick?
 15 A. I don't recall.
 16 Q. Was that discussed with
 17 Dr. Margolskee?
 18 A. I don't recall.
 19 Q. Isn't it a fact, sir, that the
 20 three of you discussed that and came to a
 21 conclusion this is what should be done?
 22 MS. DYKSTRA: Objection to the
 23 form.
 24 THE WITNESS: I have no
 25 recollection.

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1 BY MR. BEGLEITER:
 2 Q. By the way, I don't know if I
 3 asked it. Did you receive this document in
 4 the usual course of your employment?
 5 A. The document was -- let's see,
 6 am I here? Yes, the document was sent to me
 7 on October 31, 1999, and, therefore, I assume
 8 I did receive it.
 9 MS. DYKSTRA: When is a good
 10 time to take a break? I don't know if
 11 you want to go another time, we can
 12 break for lunch.
 13 MR. BEGLEITER: Let me just see
 14 what the latest one is. We can do it
 15 now.
 16 MS. DYKSTRA: Okay.
 17 MR. BEGLEITER: Have it now.
 18 MS. DYKSTRA: We'll come back.
 19 MR. BEGLEITER: Come back and
 20 then we'll go to lunch.
 21 MS. DYKSTRA: That's sounds
 22 fine.
 23 MR. BEGLEITER: Okay. Fine.
 24 VIDEOGRAPHER: The time is now
 25 12:16. Going off the video record.

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1 - - -
 2 (A recess was taken.)
 3 - - -
 4 VIDEOGRAPHER: The time is now
 5 12:31. We're back on the video record.
 6 BY MR. BEGLEITER:
 7 Q. What would have -- what, if
 8 anything, in the years '99, 2000, 2001 when
 9 you were with biologics, would have indicated
 10 to you that there was a problem with the
 11 efficacy of the vaccine?
 12 A. Nothing at all.
 13 Q. What if statistics in the field
 14 had been different?
 15 MS. DYKSTRA: Objection. Form.
 16 BY MR. BEGLEITER:
 17 Q. Well, do it this way.
 18 A. I don't know what that means.
 19 Q. On what basis -- you've said, I
 20 believe, you testified -- if I put words in
 21 your mouth, please correct me, I'm sure you
 22 will.
 23 What is the basis -- on what
 24 basis, what scientific basis do you conclude
 25 that in those years that you were biologic

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<p style="text-align: right;">Page 138</p> <p>1 that the vaccine was effective? 2 A. Well, the original basis for the 3 determination of the vaccine's efficacy or 4 efficaciousness is a controlled clinical 5 study. So that was the controlled clinical 6 study that was performed that supported the 7 original licensure of the vaccine back in 8 whenever it was, the '60s, the '70s. So that 9 was the placebo-controlled study. 10 Subsequent to that, your 11 establishment of the -- one's determination of 12 the continued effectiveness of the vaccine is 13 that, you know, when the vaccine became widely 14 used as a pediatric vaccine in this country, 15 the mumps epidemics which tended to occur with 16 certain regularity completely disappeared and 17 those epidemics have not recurred since. The 18 only way in which that would have happened is 19 if the vaccine had, in fact, retained its 20 effectiveness. 21 Q. Would a sustained outbreak short 22 of an epidemic lead you to a different 23 conclusion? 24 A. No, sustained outbreaks, the 25 problem is there are a lot of variables</p>	<p style="text-align: right;">Page 140</p> <p>1 BY MR. BEGLEITER: 2 Q. In that first paragraph again, 3 "The primary study hypothesis of a SCR greater 4 than or equal to 90 percent against wild type 5 mumps virus is unlikely to be met and 6 therefore this should be revised either in 7 terms of addressing the hypothesis or 8 addressing the technical limitations of the 9 assays used to date." [As read] 10 Your name is in this document, 11 isn't it? 12 A. Yes. 13 Q. What do you understand 14 "addressing the hypothesis" to mean? 15 A. The hypothesis of the study, so 16 that would be the 007 study, and addressing 17 the hypothesis of what the 007 study was 18 designed to do which was to provide data to 19 establish a number, potency number that could 20 be used for end expiry. And if the assay is 21 insufficiently sensitive to show statistical 22 differences in terms of seroconversion rates, 23 not effectiveness, seroconversion rates among 24 the three levels that were being tested within 25 the study, one could not appropriately address</p>
<p style="text-align: right;">Page 139</p> <p>1 associated with those. You don't know how 2 many individuals were immunized, how, many 3 individuals have not been immunized. Immunity 4 wains, goes away with time. It depends on how 5 long -- I'm slowing down, my apologies. It 6 depends on how long those individuals have 7 been immunized. It depends on a number of 8 factors which it's the only -- the only thing 9 that I personally would have taken as a clear 10 indication of the loss of effectiveness of the 11 vaccine, particularly given the fact that the 12 vaccine is used in practically every child, 13 there are unfortunately children who are not 14 immunized as we know, would be an actual 15 sustained epidemic. 16 Q. Did you -- let's go back to this 17 document for a moment. 18 A. Which document? 19 Q. This document, the one you had 20 before, I think it was 9. 21 A. Number 9? 22 Q. It's 8. 23 A. Number 8? 24 MS. MAHENDRANATHAN: It's 9. 25 MR. BEGLEITER: 9 is right.</p>	<p style="text-align: right;">Page 141</p> <p>1 the hypothesis. 2 Q. And one way of addressing the 3 hypothesis was in the choice of the viral 4 strain to be -- of the isolate to be assayed? 5 A. Not to address the hypothesis 6 but the choice of the viral strain was 7 necessary to look at how one could devise an 8 assay that would give sufficient sensitivity 9 as a measure of seroconversion. 10 Q. And did that mean, going to the 11 bottom paragraph, that Jeryl Lynn was a better 12 choice for the assay than Lo1? 13 MS. DYKSTRA: Objection to the 14 form. 15 THE WITNESS: The low passage 16 Jeryl Lynn which was, as we discussed 17 earlier, a representation of wild type 18 virus, was selected because this 19 particular strain, defined by both 20 passage and isolate, the Jeryl Lynn 21 isolate, was apparently capable of 22 giving a much more sensitive 23 representation of seroconversion, yes. 24 BY MR. BEGLEITER: 25 Q. Have you ever heard that the</p>

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1 use -- anybody at CBER ever tell you that
 2 using the low passage Jeryl Lynn was -- for
 3 this assay was stacking the deck?
 4 MS. DYKSTRA: Objection. Form.
 5 THE WITNESS: I do not recall
 6 that. But what I do recall is that
 7 these discussions of selection of --
 8 that all of the discussions involving
 9 the actual design of the assays, both
 10 the plaque reduction neutralization
 11 assay, the AIGENT assay and the
 12 subsequent ELISA assay, were all
 13 discussions that were held in
 14 collaboration with the agency and with
 15 the agency's concurrence.
 16 BY MR. BEGLEITER:
 17 Q. Do you know if London-1 was
 18 tested using all three of the potencies?
 19 A. I do not recall.
 20 Q. So leaving aside the agency,
 21 there's a question I didn't ask you, but
 22 you've said it, you're sure it happened and --
 23 A. That I recall.
 24 Q. Can you tell me what day it
 25 happened?

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1 A. I cannot tell you.
 2 Q. Who was there?
 3 A. No, I can't tell you because
 4 these were ongoing discussions with the agency.
 5 Q. So you can't identify the people
 6 at the agency. Maybe you can. Can you
 7 identify the people at the agency?
 8 A. Not at this stage.
 9 Q. Let me finish. Can you identify
 10 the people at the agency that said this is the
 11 appropriate thing to do --
 12 A. Not at this stage, no.
 13 Q. -- using Jeryl Lynn virus?
 14 A. No, I cannot identify the
 15 individuals that were involved.
 16 Q. Or any document that says it?
 17 A. I cannot at this point identify
 18 a document.
 19 Q. Who is Keith Chirgwin, Dr. Keith
 20 Chirgwin?
 21 A. Dr. Keith Chirgwin was a member
 22 of the vaccine regulatory group.
 23 Q. So he was someone -- was he on a
 24 par with you, below you, above you?
 25 A. Well, he was not within my

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1 group. So he was in not in my reporting
 2 relationship. He's a member of the vaccine
 3 regulatory group who worked with Henrietta
 4 Ukwu who was the head of vaccine regulatory.
 5 Q. Did you work with Dr. Chirgwin?
 6 A. Since he was a member of the
 7 regulatory group, as part of overall broad
 8 collaboration of the vaccine research and
 9 development, yes, I did.
 10 Q. Did you respect his opinion?
 11 A. Yes, I did.
 12 Q. I'm going to show you a
 13 document, 626382 through 626384. As you look
 14 at it, the first page does not have any
 15 e-mails to you. I'll save some time. So I'm
 16 only going to be focusing on the e-mail on the
 17 second page which I believe --
 18 - - -
 19 (Exhibit Emini-10, E-mail
 20 exchange, 00626382 - 00626384, was
 21 marked for identification.)
 22 - - -
 23 THE WITNESS: Sorry, please ask
 24 your question.
 25 BY MR. BEGLEITER:

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1 Q. I'm just letting you know I'm
 2 not going to -- you're not on the e-mails
 3 beginning on the top third of the second page,
 4 so I'm not going to ask you any questions
 5 about those e-mails. Okay?
 6 A. Okay.
 7 Q. But I will ask you about the
 8 e-mail in which your name is in the cc. Do
 9 you see that?
 10 A. Yes.
 11 Q. It's from Dr. Keith Chirgwin.
 12 A. Yes.
 13 Q. It's dated November 17, 1999.
 14 See it? Okay. And let's talk about that,
 15 about that e-mail, that first paragraph.
 16 A. Allow me time to read it,
 17 please. Okay.
 18 Q. In that paragraph can you tell
 19 me what Dr. Chirgwin is addressing?
 20 A. Well, Dr. Chirgwin is addressing
 21 the issue that we were discussing a moment
 22 ago, and that is whether or not there is
 23 relevance -- in the assay that is being
 24 developed in support of the 007 study, whether
 25 or not there is relevance to the use of wild

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<p style="text-align: right;">Page 146</p> <p>1 type strains of the virus. The argument he is 2 making is that when one uses different wild 3 type strains, not just the Lo1, there are 4 large differences that are seen in 5 seroconversion rates. And since the sera that 6 are being tested are all the same sera, it 7 would tend to suggest, not suggest, but 8 clearly shows that the differences are due to 9 the actual strains that are being used as the 10 indicator strains in the assay. 11 So, therefore, he makes the 12 conclusion that given that the vaccine 13 effectiveness is what it is observed to be, 14 very good vaccine effectiveness, since there 15 are no sustained outbreaks, that the assay 16 being developed with the different wild type 17 strains giving not just low seroconversion 18 rates but a wide variation of seroconversion 19 rates is an artifact, if you will, of the wild 20 type strains being used, and, therefore, not 21 reflective of the vaccine's effectiveness. 22 Q. A couple of questions. First of 23 all, he has a different point of view, would 24 that be fair to say, on the relevance of the 25 sustained -- of sustained outbreaks?</p> <p style="text-align: right;">Page 147</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: No, I would say 3 that that is, in fact, the same point 4 of view. 5 BY MR. BEGLEITER: 6 Q. Doesn't he say here, I'll read 7 it, "...the low SCR with wild type does not 8 correlate with the apparent field effectiveness 9 of the vaccine and the low SCR with wild type 10 has not resulted in sustained outbreaks, thus 11 these low SCRs are not capturing the true 12 protective efficacy of the vaccine." [As read] 13 A. That's exactly what I said 14 before. 15 Q. Well, you drew a distinction, 16 did you not, between epidemics and sustained 17 outbreaks? 18 A. Well, his definition of 19 sustained outbreaks, all right, and the way 20 he's defining it here is equivalent to my 21 definition of an epidemic. 22 Q. How do you know that? 23 A. Well, because what he's 24 referring to is -- because an epidemiologist 25 would all refer to it as exactly the same way.</p>	<p style="text-align: right;">Page 148</p> <p>1 What he's referring to -- what I refer to as 2 an epidemic is a widespread sustained outbreak 3 that would typically occur across all children 4 of a given age who have received vaccine at 5 the time that they were -- or received lots of 6 vaccine that were presumably no longer 7 effective at the time that they hit that age 8 when they would normally receive the vaccine. 9 So these children would all grow up at the 10 same time and then you would see an epidemic 11 within that age band. That is a sustained 12 outbreak. We've not seen that with mumps. 13 Q. You're not trained in epidemiology, 14 are you? 15 A. I am -- well, my training is 16 very broad and, in fact, in my current role, 17 okay, I do field effectiveness studies, yes. 18 Q. You know what Dr. Chirgwin of 19 sustained outbreaks is? 20 A. Well, without having spoken to 21 him, I interpret it the way I just mentioned. 22 Q. He doesn't in this -- you 23 haven't seen anywhere where he says a 24 sustained outbreak is blumpity-blump? 25 MS. DYKSTRA: Objection to the</p> <p style="text-align: right;">Page 149</p> <p>1 form. 2 THE WITNESS: Of course not. 3 BY MR. BEGLEITER: 4 Q. Okay. Fine. Well, I want to 5 make sure we're on the same thing, may have 6 missed it. 7 And then in the last sentence, 8 "If these arguments fail and CBER forces us to 9 use wild type neutralization, then we will 10 argue that 70 to 80 percent of SCR with Lo1 11 correlates with excellent field effectiveness 12 and that therefore this is an acceptable SCR." 13 [As read] 14 Do you see that? 15 A. Yes. 16 Q. Do you agree with that? 17 A. It's the only argument that one 18 can make. So if the agency is insisting that 19 the London-1 strain, which is what Lo1 20 apparently stands for, has to be used in the 21 assay because it is a wild type virus, we know 22 that the effectiveness of the vaccine is at a 23 very high level, much higher than what would 24 be reflected in an assay using the Lo1 strain 25 which is on the order of, as noted here, 70 to</p>
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<p style="text-align: right;">Page 150</p> <p>1 80 percent, then the conclusion would be that 2 what you are measuring in the assay at a level 3 of 70 to 80 percent using the Lo1 strain is a 4 reflection of the vaccine's known and observed 5 field effectiveness. 6 Q. And coming back to the premise 7 of what you just said, do you know what the 8 agency, what CBER was requiring in terms of -- 9 A. CBER was requiring -- 10 Q. -- in terms of seroconversion 11 rate? 12 A. CBER was requiring an assay of 13 sufficient sensitivity. And based on the 14 documents that I reviewed recently, they were 15 requiring a level of sensitivity, of 16 seroconversion rate of at least 90 percent as 17 that would allow you a sufficient sensitivity 18 to address the hypothesis that was being 19 addressed in the 007 trial. 20 Q. The documents that I showed you 21 this morning? 22 A. No, the documents that I 23 reviewed with my counsel over the past several 24 days. 25 Q. Do you know what the document</p>	<p style="text-align: right;">Page 152</p> <p>1 rates that could address the hypotheses 2 of the 007 trial. 3 BY MR. BEGLEITER: 4 Q. Which included a 90 -- an equal 5 to or greater than 90 percent seroconversion 6 rate? 7 A. Which included a seroconversion 8 rate of 90 percent, at least a seroconversion 9 rate of 90 percent. 10 Q. What would a low seroconversion 11 rate have meant to shelf life -- 12 MS. DYKSTRA: Objection. Form. 13 BY MR. BEGLEITER: 14 Q. -- if anything? 15 A. Again, it's not what the 16 seroconversion rate means to shelf life. It's 17 what the difference in seroconversion rates 18 might mean based upon a prespecified criterion 19 when the results from the 007 trial would 20 ultimately be evaluated and become available. 21 Q. This morning, I hope it's still 22 morning, this morning you talked about how 23 everything pharmaceutical decays over time? 24 A. Right. 25 Q. And stabilizers is sometimes put</p>
<p style="text-align: right;">Page 151</p> <p>1 is? 2 A. There were multiple documents. 3 I can't recall off the top of my head, but 4 there were multiple documents that referred to 5 the need of having an assay with sufficient 6 sensitivity -- there were multiple documents 7 that referred to the need to have an assay 8 that demonstrated at least 90 percent 9 seroconversion. 10 Q. So the -- I think we'll get off 11 the subject. Did Merck test the Protocol 007 12 serum samples against London-1? 13 A. I don't recall if the tests 14 against London-1 were done with the Protocol 15 007 serum samples or with samples from other 16 studies. 17 Q. So is it fair to say that in 18 designing Protocol 007, that the assay that 19 was chosen was an assay which gave Merck a 20 likelihood of getting the seroconversion rate 21 that CBER wanted? 22 MS. DYKSTRA: Objection. Form. 23 THE WITNESS: Both assays, the 24 PRN assay and the ELISA assay were 25 designed to give rise to seroconversion</p>	<p style="text-align: right;">Page 153</p> <p>1 into vaccines -- 2 A. Correct. 3 Q. -- to retard degradation? 4 A. Into any pharmaceutical product. 5 Right. 6 Q. And we now know, you've told us, 7 that there was a fill to 5.0 log? 8 A. Right. 9 Q. And the point of the end expiry 10 test was to see whether or not that would 11 be -- that it would meet, that the vaccine 12 would meet CBER's requirements at the end of 13 expiry. Right? 14 MS. DYKSTRA: Objection. Form. 15 THE WITNESS: No. What it would 16 mean -- no. So CBER established a 17 requirement that the 4.3 potency value 18 in the label, the vaccine's label 19 should appropriately be considered to 20 be, should be considered to be, this 21 was CBER's declaration, should be 22 considered to be the potency value at 23 the end of the vaccine's shelf life. 24 That's what the agency declared. 25 BY MR. BEGLEITER:</p>

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1 Q. Who is Philip Bennett?
 2 A. I don't recall his exact
 3 position within the company. He's not within
 4 the company. Actually I don't recall exactly.
 5 Q. Did --
 6 A. I really don't.
 7 Q. Was there statisticians who
 8 would review at Merck the results of clinical
 9 trials?
 10 A. Any clinical trial is a
 11 statistically driven study, yes. Yes.
 12 Q. I'd like to show you this
 13 particular document which bears numbers
 14 MRK-0562218 and 19. Let me distribute it
 15 right now.
 16 - - -
 17 (Exhibit Emini-11, 3/14/01
 18 E-mail with attachment, 0562218 &
 19 0562219, was marked for identification.)
 20 - - -
 21 THE WITNESS: Okay.
 22 BY MR. BEGLEITER:
 23 Q. You see on page 2, the second
 24 page has a chart, a table. Do you see that?
 25 A. Uh-huh.

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1 Q. And this doctor makes the
 2 following statement with regard to that table.
 3 A. Right.
 4 Q. He says, "Following are the loss
 5 and variability estimates for mumps at various
 6 time points."
 7 A. Right.
 8 Q. "Our expiry dating needs to be
 9 12 months in order to provide 95 percent
 10 confidence that a lot released at 5.0 will be
 11 above 4.3 at expiry."
 12 Do you see that?
 13 A. Yes.
 14 Q. What does that mean to you?
 15 A. That means by looking at the
 16 available stability data that was available to
 17 Phil Bennett at the time and then modeling
 18 that data on a statistical model, he comes to
 19 the conclusion that if we establish 4.3 as an
 20 expiry dating and you fill with a potency of
 21 5, that there is -- that if you want to be
 22 guaranteed with a 95 percent probability, that
 23 you will be at the end of shelf life at 4.3
 24 starting at 5, okay, then the length of that
 25 shelf life can be no more than 12 months.

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1 Q. And if the shelf life instead
 2 was, as you speculate is possible, you didn't
 3 testify definite but it could be as much as
 4 two years, you said?
 5 A. It could be as much as two
 6 years.
 7 Q. That would be beyond the shelf
 8 life of the --
 9 A. No, that would be beyond --
 10 Q. Let me finish the sentence.
 11 -- beyond the shelf life intended?
 12 A. None of this declares shelf
 13 life. What this only says is that based on
 14 statistical modeling, if I start at 5 and want
 15 to end at 4.3 and I want to do that with a 95
 16 percent probability, I probably should go no
 17 longer than 12 months.
 18 Q. Now, if the expiry that CBER
 19 wanted could only be maintained for 12 months,
 20 wouldn't that mean that a shelf life
 21 afterward, after 12 months -- well, what would
 22 that mean to a shelf life that -- excuse me,
 23 withdraw the question.
 24 If a determination was made by
 25 Merck that 4.3 log 50 dose would only support

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1 12-month expiry using -- what would that mean
 2 to shelf life, if anything?
 3 MS. DYKSTRA: Objection. Form.
 4 THE WITNESS: Are you referring
 5 specifically to this note as a
 6 determination?
 7 BY MR. BEGLEITER:
 8 Q. No, I'm asking you as a general
 9 question.
 10 A. If a determination were made,
 11 well, so if the agreement, if there is an
 12 agreement with the agency that the end expiry
 13 potency should be X, whatever the number is,
 14 and if a formal determination and a formal
 15 stability study shows that at a given time
 16 point you are highly likely to be below X,
 17 that does define your shelf life in general
 18 sense.
 19 Q. Let me ask you some questions
 20 and then maybe we'll go to lunch.
 21 Were you involved with hiring
 22 and firing people in your division?
 23 A. I did not hire and fire
 24 directly. That was the responsibility of HR
 25 and the responsibility of my senior staff.

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1 Q. Was your signature necessary to
 2 hire someone?
 3 MS. DYKSTRA: Objection.
 4 THE WITNESS: It depends on the
 5 level of the individual that came in.
 6 BY MR. BEGLEITER:
 7 Q. Let's say Mr. Krahlung here.
 8 A. I don't recall what level he
 9 came in.
 10 Q. How about terminating someone,
 11 did you have a responsibility to sign off on a
 12 termination?
 13 MS. DYKSTRA: Objection.
 14 THE WITNESS: It depended on the
 15 nature of the termination. But, again,
 16 most terminations were handled directly
 17 through HR and legal.
 18 BY MR. BEGLEITER:
 19 Q. How about when Mr. Krahlung left
 20 Merck, did you sign off on a document?
 21 A. I have no recollection.
 22 MS. DYKSTRA: Let him finish the
 23 question.
 24 THE WITNESS: I'm sorry.
 25 BY MR. BEGLEITER:

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1 Q. I'd like to show you -- withdrawn.
 2 When Dr. Krahlung wanted to hire
 3 somebody, a virologist such as Stephen Krahlung
 4 or someone else, was your approval necessary?
 5 A. I have no direct recollection,
 6 but it would be highly unlikely that my
 7 approval would be necessary.
 8 Q. Would he be consulting with you
 9 as to whether or not to hire someone?
 10 MS. DYKSTRA: Objection.
 11 THE WITNESS: The consultation
 12 would probably have been -- probably
 13 have been most likely with Dr. Shaw.
 14 BY MR. BEGLEITER:
 15 Q. Let's take a look at this.
 16 Merck 331424 to 33. This is Emini-12.
 17 - - -
 18 (Exhibit Emini-12, 10/10/00
 19 Memo, 00331424 - 00331433, was marked
 20 for identification.)
 21 - - -
 22 THE WITNESS: Okay.
 23 BY MR. BEGLEITER:
 24 Q. My question to you is, does this
 25 refresh your recollection that you were

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1 involved with the hiring one way or another of
 2 Stephen Krahlung?
 3 A. It doesn't refresh my recollection
 4 of the day that this was received, but I will
 5 agree that this was sent to me, likely
 6 received by me and that I likely may have read
 7 it.
 8 Q. In the last paragraph on the
 9 second page, "I therefore recommend offering
 10 one of our remaining technical positions to
 11 Steve."
 12 Do you see that?
 13 A. Yes.
 14 Q. And did you act on that
 15 recommendation?
 16 A. I don't recollect if I acted on
 17 that recommendation directly or discussed it
 18 with Dr. Shaw and allowed him to make the
 19 final determination.
 20 Q. Did you receive this document in
 21 the usual course of your employment?
 22 A. I will assume that I did because
 23 it was addressed to me.
 24 Q. Do you have any reason why you
 25 wouldn't have received it, you know of no

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1 reason?
 2 A. I know of no reason why I would
 3 not have received it.
 4 MR. BEGLEITER: Let's have it as
 5 Number 13.
 6 - - -
 7 (Exhibit Emini-13, Resignation
 8 Authorization Form, 00582392, was
 9 marked for identification.)
 10 - - -
 11 BY MR. BEGLEITER:
 12 Q. Okay. Doctor, is your signature
 13 on this page?
 14 A. Yes, it is.
 15 Q. And you signed in the usual
 16 course of your employment?
 17 A. Yes, I did.
 18 Q. And it's signed 12/20/01. Do
 19 you see that?
 20 A. Yes.
 21 Q. You indicated, I believe, a few
 22 minutes ago, again, if I got it wrong, please
 23 tell me, that you didn't sign off on every
 24 resignation or termination?
 25 A. I said I didn't recollect if I

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<p style="text-align: right;">Page 162</p> <p>1 signed off on everyone's resignation. So I 2 don't know -- I mean, this was obviously a -- 3 could have been a process that was in place 4 which I have no recollection of at Merck at 5 the time that all resignations were signed off 6 by the appropriate HR person that was the 7 other signature on this and the head of the 8 department would have been me. 9 Q. That person is Robert Suter? 10 A. From HR, yes. 11 Q. And he wasn't a doctor? 12 A. No. 13 Q. Do you know what position 14 Mr. Suter held at HR? 15 A. The exact level of his position, 16 I don't know. But he was assigned as the 17 senior HR person to the -- to my department. 18 Q. How many -- was Steve Krahling's 19 title virologist, to your recollection? 20 A. I don't recollect the exact 21 title. 22 Q. What were the titles of the 23 people who worked in -- who worked on Protocol 24 007 with Dr. -- 25 A. I don't recollect the exact</p>	<p style="text-align: right;">Page 164</p> <p>1 Q. How about Frank Kennedy? 2 A. Frank Kennedy, I did see the 3 name when reviewing documents, but actually I 4 have -- that's a recollection that hasn't even 5 come back. I don't recognize it at all. 6 Q. How about Joan Wlochowski? 7 A. First name, please? 8 Q. Joan? 9 A. Joan. Joan Wlochowski. 10 Q. W-L-O-C-H-O-W -- 11 A. Yes. Yes, I do recall. Yes, I 12 do recall. 13 Q. We're talking together, it's 14 going to drive her crazy. 15 A. My apologies. 16 Q. Joan W-L-O-C-H-O-W-S-K-I? 17 A. Yes. 18 Q. What do you recall about her? 19 A. Same thing. You know, same 20 level with Mr. Krahling and then with Mary 21 Yagodich, you know, in the laboratory. The 22 laboratory operational staff under Dr. Krah. 23 Q. How many people worked in -- how 24 many professionals worked in the laboratory? 25 MS. DYKSTRA: Objection.</p>
<p style="text-align: right;">Page 163</p> <p>1 titles. Too many companies in between and too 2 many different titles. 3 Q. Do you have any recollection as 4 to who worked in that lab other than Dr. Krah 5 and Steve Krahling? 6 A. Recollections only came back 7 when reviewing documents over the past several 8 months and seeing various names being present. 9 Q. Okay. Let me just throw some 10 names out and see if you recollect them. Mary 11 Yagodich? 12 A. Yagodich I do recall, yes. 13 Q. What was her -- what do you 14 recall about her? 15 A. I mean, to my recollection, 16 under David Krah, so she was a member of David 17 Krah's laboratory. My recollection is that 18 practically everyone in the laboratory under 19 David Krah had worked at the same level, but I 20 can't attest to that being the fact. It could 21 be, one could have been slightly higher, one 22 below, I don't know. 23 Q. Do you know if she was his 24 second in command? 25 A. I don't recall.</p>	<p style="text-align: right;">Page 165</p> <p>1 THE WITNESS: I believe there 2 were four or five. 3 BY MR. BEGLEITER: 4 Q. Tell me, sir, do you know during 5 the time of Protocol 007 if any of the women 6 working in the lab were pregnant? 7 A. I don't recall. 8 Q. Was there a rule in the lab that 9 pregnant women couldn't work near live viruses? 10 A. That was a general rule, 11 absolutely. Still is. 12 Q. Let me see if I can refresh your 13 memory. I'm going to show you Merck 14744 14 through 747. We'll mark this now as 13. 15 MS. DYKSTRA: 14. 16 MR. BEGLEITER: 14. 17 - - - 18 (Exhibit Emini-14, 3/29/01 Memo, 19 00014744 - 00014747, was marked for 20 identification.) 21 - - - 22 THE WITNESS: Yes, I do recall 23 this memo. In fact, this is a memo 24 that I did review recently now that I 25 see it, yes. Thank you.</p>

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<p>1 BY MR. BEGLEITER: 2 Q. And did you receive this memo in 3 the usual course of your employment? 4 A. Yes, I did. 5 Q. And does that indicate in the 6 second page that Mary is the -- 7 A. Mary Yagodich in seventh month 8 of pregnancy. 9 Q. That's as of March 29, 2001? 10 A. Yes. 11 MS. DYKSTRA: Just for the 12 record, I have two memos. Did you mean 13 to give two memos? 14 MR. BEGLEITER: Are they both 15 Mary Yagodich? 16 MS. DYKSTRA: They are both Mary 17 Yagodich. 18 MR. BEGLEITER: I didn't mean to 19 give you two but -- 20 MS. DYKSTRA: They're different 21 memos, though. 22 THE WITNESS: Yeah, they are 23 different. 24 BY MR. BEGLEITER: 25 Q. The 746, I'll use that later.</p>	<p>1 - - - 2 BY MR. BEGLEITER: 3 Q. We used them. Sorry. I 4 apologize. That should be stricken I believe. 5 Well, we'll leave it marked, we'll use it 6 anyway, but not right now. I wanted to show 7 you something else. 8 A. Okay. 9 Q. This document would not indicate 10 that Mr. Krahling was pregnant. 11 A. No, it would not. 12 Q. Jennifer Kriss, okay. 13 MR. BEGLEITER: I'd like to have 14 marked 15719 to 15720. 15 - - - 16 (Exhibit Emini-16, 3/29/01 Memo, 17 00015719 & 00015720, was marked for 18 identification.) 19 - - - 20 BY MR. BEGLEITER: 21 Q. So this memo involves Jennifer 22 Kriss. Is that right? 23 A. Yes, it does. 24 Q. And who was Jennifer Kriss, do 25 you know?</p>
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<p>1 If you can hand that back to me, I appreciate 2 it. 3 MS. DYKSTRA: Bob, can I have 4 that copy back then, the one you're 5 using? 6 MR. BEGLEITER: Yes. It should 7 be during the course of the year 2000. 8 That's how it should begin. 9 MS. DYKSTRA: Ending in 14744 as 10 the Bates number? 11 MR. BEGLEITER: Yes. 12 MS. DYKSTRA: Thank you. 13 BY MR. BEGLEITER: 14 Q. You did receive this and 15 acknowledge that she was pregnant March 29, 16 2001? 17 A. That's what it says. 18 Q. And does this also refresh your 19 recollection about -- forget it. 20 MR. BEGLEITER: Can you mark 21 15702 to 03 as number 15, Emini-15? 22 - - - 23 (Exhibit Emini-15, 3/29/01 Memo, 24 00015702 & 00015703, was marked for 25 identification.)</p>	<p>1 A. Jennifer Kriss I recall as being 2 a member of the laboratory. 3 Q. Dr. Krah's lab? 4 A. Dr. Krah's laboratory. 5 Q. This was sent to you in the 6 usual course of your employment? 7 A. Yes, it was. 8 Q. Was she also pregnant? 9 A. According to the memo, she was 10 in the fifth month of her pregnancy, and it's 11 dated 29 March 2001. 12 Q. Going to the previous one, which 13 was the one that was inadvertently marked 14 involving Stephen Krahling but dated the same 15 day. 16 A. Yes. 17 Q. Did you receive that in the 18 usual course of your employment? 19 A. Yes, I did. 20 Q. Now, all of these are dated 21 March 29th? 22 A. Yes. 23 Q. Talk about Protocol 005. Is 24 that -- what is -- were any of these people 25 working on Protocol 005?</p>

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<p style="text-align: right;">Page 170</p> <p>1 A. Well, it refers to Protocol 005. 2 What I do not recall and don't know at the 3 moment was whether or not Protocol 005 was the 4 laboratory number for the assays that were 5 being done in support of the clinical study in 6 Protocol 007. That, I don't recall. So we 7 would need to look at what Protocol 005 8 actually refers to. 9 Q. The point being is that if you 10 look at any of those, can you tell whether or 11 not these people were working on Protocol 007? 12 A. Well, all of these refer to the 13 neuts of the mumps neut assay, and in one case 14 it refers to 570 serum pairs were tested in 15 emergency response to CBER's citation during 16 the MMD. But it doesn't say, I can't tell you 17 if it was 007 or something different. I 18 cannot tell from this. 19 Q. You can't tell whether or not in 20 that first paragraph, I believe they're all -- 21 take a look at the one regarding Mary 22 Yagodich, she was working on -- 23 A. This refers to two sets of 24 assessments, one was the development of an 25 assay that was then used to assess the sera in</p>	<p style="text-align: right;">Page 172</p> <p>1 by the agency with respect to end expiry, but 2 I don't recollect the details of those 3 assessments. 4 Q. Ms. Yagodich is in 14744. It 5 says, "In the middle of this activity we 6 received an FDA mandate to define an 7 end-expiry dose of mumps virus in MMR II." 8 A. Where are you? 9 Q. The middle of 14744. 10 A. Right. 11 Q. Sir, doesn't that refer to the 12 mandate which resulted in the Protocol 007? 13 A. It may, but I cannot, again, 14 based on this language, make a direct 15 determination. 16 On the second sentence it refers 17 to "...an interim set of data in time for a 18 projected meeting with the FDA." There was an 19 interim analysis that was performed in 007, so 20 this may refer to it. 21 Q. I'll put it to you this way: 22 This is Yagodich, going to the Krahlung one, 23 can you think of any other protocol other than 24 007 in which this document would indicate he 25 was working on?</p>
<p style="text-align: right;">Page 171</p> <p>1 the head-to-head clinical study of MMR II and 2 Priorix, as we discussed before. It does not 3 indicate whether or not that assay was 4 actually run in the laboratory here or just 5 solely developed, which normally would have 6 been the case. The assay would have been run 7 in a different laboratory. And then it also 8 refers to data that needed to be generated to 9 address a question that came up with respect 10 to end expiry and shelf life to end expiry. 11 Q. And that would be 007. Is that 12 right? 13 A. I can't tell exactly from the 14 terminology used in this memo whether we're 15 referring specifically to 007 or to something 16 else. That, I don't recollect. 17 Q. Now, I thought I asked you 18 before whether or not there were any other end 19 expiry studies done other than 007 for mumps, 20 and you said you knew of no others? 21 A. I don't recollect that there 22 were any -- well, that there were any specific 23 clinical studies that were done. There may 24 have been assessment of sera to generate data 25 in support of questions that may have come up</p>	<p style="text-align: right;">Page 173</p> <p>1 MS. DYKSTRA: Objection. Form. 2 THE WITNESS: I cannot, no. 3 BY MR. BEGLEITER: 4 Q. Same thing with Ms. Kriss, take 5 a look at -- 6 A. You mean other than the 007? 7 Q. Other than 007. 8 A. Other than 007, from the 9 terminology in these memos, I can't conclude -- 10 Q. I asked you another question. 11 Can you think of any other protocol -- 12 A. No, I cannot. 13 Q. Let me finish. 14 Can you think of any other 15 protocol that they could have been working on 16 other than 007? 17 A. It depends. It's the definition 18 of working on that's causing me to hesitate. 19 What do you mean by "working on," developing 20 an assay or actually generating the clinical 21 data using the assay? 22 Q. The latter. 23 A. Generating the clinical data 24 using the assay. The only one I am aware of 25 is 007.</p>

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<p style="text-align: right;">Page 174</p> <p>1 Q. Now, in the years that you were 2 at biologics and vaccines, how often did Merck 3 outsource clinical trials approximately? 4 MS. DYKSTRA: Objection. Form. 5 THE WITNESS: Outsource, sorry, 6 you need more specificity. What do you 7 mean by "outsource clinical trial"? 8 BY MR. BEGLEITER: 9 Q. Well, let me ask you this, go 10 right to the subject. Do you know who Dick 11 Ward is? 12 A. Yes, I know Dick Ward. 13 Q. Who is Dick Ward? 14 A. Dick Ward was a professor of 15 virology. I don't know where he was at the 16 time. When I knew him he was at University of 17 Cincinnati, if I remember correctly. 18 Q. Do you know what hospital he was 19 associated with? 20 A. I don't remember the exact title 21 of the hospital. 22 Q. Have you ever heard of the 23 Children's Hospital Medical Center in 24 Cincinnati? 25 A. Yes, I have certainly heard of</p>	<p style="text-align: right;">Page 176</p> <p>1 the assay, how is it accomplished? What would 2 the virologist do to see if -- what the 3 reaction was? 4 A. I can't tell you what the exact 5 details were, but there were -- but there was 6 clearly a standard operating procedure 7 because, remember, the assay required to be 8 validated, so what was validated was defined 9 by the standard operating procedure. So 10 whether a validated assay, by definition, 11 doesn't matter where you run it and who runs 12 it, it will generate the same set of data. 13 Q. Well, are you saying in all 14 circumstances it would represent the -- it 15 would result in the same set of data? 16 A. Only if one could validate that 17 the laboratory that was run -- because in 18 addition to validating the assay, the 19 laboratory needs to be validated as well. 20 Q. If you were to have -- if you 21 were to hire, retain, I don't know what the 22 right word is -- 23 A. Yes, I would validate the 24 laboratory. 25 MS. DYKSTRA: Let him finish the</p>
<p style="text-align: right;">Page 175</p> <p>1 it. 2 Q. Is it a reputable hospital, 3 medical center? 4 A. Well, yes, of course. Yes. 5 Q. Was there any thought about 6 outsourcing to Dr. Ward any part of the 7 clinical trial -- 8 MS. DYKSTRA: Objection to form. 9 BY MR. BEGLEITER: 10 Q. -- of 007? 11 A. It was not to outsource the 12 clinical trial. It would have been -- 13 outsourced would have been the conduct of the 14 assays in support of the clinical trial, to 15 generate the data from the clinical trial. 16 Q. When you say "conduct of the 17 assays," what are you referring to? What 18 actual work is done to conduct the assay? 19 A. Well, it is the assay that -- 20 the assays that are designed to generate the 21 data from the clinical studies. So in the 22 context of 007 that would have been the PRN 23 assay and maybe possibly the ELISA. I don't 24 recall if it was both or just one. 25 Q. Let's talk about the PRN. To do</p>	<p style="text-align: right;">Page 177</p> <p>1 question. 2 THE WITNESS: My apologies. 3 BY MR. BEGLEITER: 4 Q. It would be validated before the 5 -- any part of the clinical trial was sent to 6 that laboratory? 7 A. Yes. 8 Q. You wouldn't have a clinical 9 trial, if that's the right word, the actual -- 10 A. Samples. 11 Q. -- samples in a place where the 12 validation had not occurred yet? 13 A. Well, you could have the samples 14 in a place where the validation had not 15 occurred yet. To actually run the assays 16 using those samples to generate the data for 17 the clinical trial purposes, typically, 18 actually, you would not do that unless you 19 were comfortable that the assay as well as the 20 facility had been appropriately validated. 21 Q. So nothing would go to 22 Dr. Ward's lab unless the facility itself was 23 validated? 24 MS. DYKSTRA: Objection. 25 Misstates his testimony.</p>

45 (Pages 174 - 177)

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<p style="text-align: right;">Page 178</p> <p>1 THE WITNESS: No. I don't 2 recall if samples had been sent to 3 Dr. Ward's laboratory, but, again, it 4 is not whether or not the samples were 5 there, it's whether or not they would 6 be running the assay. 7 BY MR. BEGLEITER: 8 Q. So go back to something I asked 9 you before. Were you contemplating using 10 Dr. Ward's lab for any purpose regarding 007? 11 A. Not that I recollect, other than 12 the review of the document showed that we were 13 clearly apparently contemplating the use of 14 Dr. Ward's laboratory as an additional 15 laboratory or as the laboratory that would run 16 the 007 samples. 17 Q. What documents were those? 18 A. Those were various documents and 19 memo that I reviewed. I cannot tell you the 20 specifics ones. 21 Q. You cannot because you don't 22 remember or because you're -- 23 A. No, I don't remember. I just 24 saw them and gave them back. I did not retain 25 anything.</p>	<p style="text-align: right;">Page 180</p> <p>1 by many years. 2 - - - 3 (Exhibit Emini-17, 2/26/09 Press 4 release, was marked for identification.) 5 - - - 6 BY MR. BEGLEITER: 7 Q. If you take a look at that, is 8 there any doubt in your mind that the Bill & 9 Melinda Gates Foundation would have given a 10 grant to the Children's Hospital of 11 Cincinnati? 12 MS. DYKSTRA: Objection. 13 THE WITNESS: Well, they did 14 give a grant. 15 BY MR. BEGLEITER: 16 Q. Okay. The place you're now 17 working, that's a reputable institution? 18 A. An exceptionally reputable 19 institution. 20 Q. And they wouldn't be giving 21 grants to people that weren't reputable? 22 A. It depends on the nature of the 23 work that needs to be done. Certainly 24 reputable in the context for which the grant 25 was given, the answer is yes.</p>
<p style="text-align: right;">Page 179</p> <p>1 Q. Now, did Dr. Ward himself have a 2 good reputation? 3 A. Dr. Ward definitely had a good 4 reputation. 5 Q. And did the hospital have a good 6 reputation? 7 A. The hospital has a good reputation. 8 Q. And you work at the Bill & 9 Melinda Gates Foundation? 10 A. Yes. 11 Q. Does the Bill & Melinda Gates 12 Foundation give grants to that hospital? 13 A. I don't know if we do or don't. 14 We give lots of grants. 15 MR. BEGLEITER: This is 17 now. 16 This does not have Bates numbers. I'll 17 describe it as what appears to be a 18 press release, dated Thursday, 19 February 26, 2009, entitled "Cincinnati 20 Children's receives \$6.7 million grant 21 from Gates Foundation to study 22 influenza vaccine in pregnant women in 23 Asia." This is before you got to 24 the -- 25 THE WITNESS: Well before, yes,</p>	<p style="text-align: right;">Page 181</p> <p>1 Q. Now, did you ever have a 2 discussion with Dr. Krah and Dr. Shaw as to 3 whether or not they would have -- well, do one 4 at a time -- with Dr. Krah as to whether or 5 not he would have preferred to do the PRN or 6 have it outsourced? 7 MS. DYKSTRA: Objection. 8 THE WITNESS: I don't recall 9 such a conversation. 10 BY MR. BEGLEITER: 11 Q. How about a conversation with 12 Dr. Shaw? 13 A. I don't recall. 14 MS. DYKSTRA: Bob, let us know 15 if it's a good time to break for lunch, 16 either before or after you finish up. 17 MR. BEGLEITER: Give me another 18 five minutes, then we'll go. Okay? 19 MS. DYKSTRA: Good. 20 BY MR. BEGLEITER: 21 Q. Let me ask it this way: Did you 22 want Merck -- would you have preferred to have 23 Merck do the PRN or have it outsourced when 24 you first learned that CBER was requiring a 25 PRN?</p>

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<p style="text-align: right;">Page 182</p> <p>1 MS. DYKSTRA: Objection. Form. 2 THE WITNESS: It doesn't matter. 3 What matters is whether or not the 4 validated assay can be run in a 5 validated laboratory. It doesn't 6 matter if it's internal or external. 7 What usually drove the decision was 8 usually a capacity decision. Assuming 9 that there was appropriate validation. 10 BY MR. BEGLEITER: 11 Q. Capacity in what sense? 12 A. Capacity in that there are just 13 so many people in a day and the facility is 14 only so large and there are a certain number 15 of samples that need to be run, so one can run 16 them. Oftentimes a good reason for 17 outsourcing an assay is because you need to 18 have additional capacity to do it. But, 19 again, the critical aspect of it is that the 20 laboratory to whom you are outsourcing the 21 assay is appropriately validated and can 22 demonstrate that it can run the assay the way 23 you would have run the assay. 24 Q. Let's go back to 14. 25 A. 14?</p>	<p style="text-align: right;">Page 184</p> <p>1 A. That would indicate that was a 2 tight capacity, so, therefore, it would be 3 have been, if appropriate, to send it to an 4 outside laboratory to expand the capacity, 5 yes. 6 Q. We've already discussed, I hope 7 we remember this, that two of the members of 8 the staff, Mary Yagodich and Jennifer Kriss 9 were pregnant and couldn't be near the live 10 vaccine. 11 A. And could not be near the live 12 varicella. 13 Q. Right. 14 A. They could still work in the 15 laboratory but not run the actual assays with 16 the live virus. 17 Q. Right. So that you assured to. 18 So weren't those reasons to outsource it, 19 those reasons -- 20 A. Any capacity. 21 MS. DYKSTRA: Let him finish the 22 question so we can make sure the record 23 is clear. 24 THE WITNESS: Sorry. 25 MS. DYKSTRA: That's okay.</p>
<p style="text-align: right;">Page 183</p> <p>1 Q. Yes, the Mary Yagodich. I'd 2 like to read a sentence to you. 3 A. Please. 4 Q. The first sentence of the second 5 paragraph. 6 A. Please. 7 Q. "The lab staff worked nights and 8 weekends across the Thanksgiving, Christmas 9 and New Year holidays in order to meet the 10 deadlines imposed on them." 11 A. Yes. 12 Q. This is 2000 -- this memo is 13 dated March 29, 2001? 14 A. Yes. 15 Q. "The plan for the remaining 16 samples had...", Dr. Shaw emphasizes it. 17 A. Yes. 18 Q. "...had been to send them to an 19 outside contract laboratory." 20 Do you see that? 21 A. Yes. 22 Q. Was the conditions in the lab 23 among the workers having to work Thanksgiving 24 and Christmas and New Year's a factor in 25 deciding to send it to an outside lab?</p>	<p style="text-align: right;">Page 185</p> <p>1 BY MR. BEGLEITER: 2 Q. So that was a reason to do it? 3 A. Yes. 4 Q. But a decision was made not to 5 outsource. Right? 6 MS. DYKSTRA: Objection. 7 THE WITNESS: The decision was 8 made not to outsource. 9 BY MR. BEGLEITER: 10 Q. That decision was made by you, 11 was it not? 12 MS. DYKSTRA: Objection. 13 THE WITNESS: I don't recall if 14 I made that decision or not. However, 15 in reading the memo, it was indicated 16 that the reason why the decision, that 17 was the next sentence after the 18 sentence that you note, not to 19 outsource it was concern that the 20 outsourcing laboratory, which 21 presumably was Dr. Ward's laboratory, 22 was not capable of reproducing the 23 required precision that would be 24 needed. 25 BY MR. BEGLEITER:</p>

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<p style="text-align: right;">Page 186</p> <p>1 Q. Where does it say capable? 2 A. Well, it just says -- 3 Q. It says not be able to 4 reproduce. 5 A. Well, I read it as capable. You 6 may read it as not being able to reproduce the 7 precision. So there was a concern obviously 8 that they could not reproduce the precision. 9 Q. Didn't we discuss like a half an 10 hour ago that if the lab was validated, two 11 labs validated the same way doing the same 12 protocols would come up with the same results? 13 A. If the assay is validated, yeah. 14 If the assay and the laboratory are validated. 15 So there was obvious concern over the 16 validation of the laboratory. 17 Q. Where does it say that? 18 MS. DYKSTRA: Objection. 19 THE WITNESS: Where does it not 20 say that? 21 BY MR. BEGLEITER: 22 Q. Okay. But where does it say it, 23 sir? 24 A. Well, it doesn't say. 25 MS. DYKSTRA: Objection.</p>	<p style="text-align: right;">Page 188</p> <p>1 what he was referring to is the fact that the 2 data generated using the samples that had been 3 tested to date yielded values that were very 4 tight with each other and, therefore, with a 5 very narrow confidence interval. When you see 6 that, it is imperative that you be certain, 7 particularly if you're going to a different 8 laboratory, that the validation of that 9 laboratory be very good because the precision 10 of the assay, which is the most difficult 11 characteristic of an assay to control, is well 12 controlled, particularly for a biological 13 assay. 14 Q. Are you speculating here this 15 afternoon that Dr. Ward's lab would not have 16 had the proper validation? 17 A. What I am saying is that at the 18 time that this decision was made and given the 19 time constraints that were involved, that 20 either there was a concern, that there was a 21 concern either based on observation or simply 22 based on principle, that Dr. Ward's lab might 23 not be able to run the assay in a way that 24 would ensure the same level of required 25 precision.</p>
<p style="text-align: right;">Page 187</p> <p>1 BY MR. BEGLEITER: 2 Q. Go ahead, I'm sorry. 3 A. Just slow down for a second. 4 Q. Okay. 5 A. Tell me when you're ready. Ready. 6 It doesn't say it, but in 7 reading the documents, the suggestion was, and 8 again, I have no direct recollection, to not 9 to send it to Dr. Ward's laboratory either 10 because it had not yet been validated and 11 brought under time pressure to generate the 12 data so, therefore, the decision was made to 13 keep it entirely internally and to deal the 14 best that one could with the capacity issue, 15 which is what is reflected in these documents; 16 or alternatively, to deal the best that we 17 could with the capacity issue because there 18 was concern over the quality of the data that 19 would be generated in Dr. Ward's laboratory. 20 Q. What did you understand Dr. Shaw 21 to mean when he said tightness of the data? 22 A. The precision of the data. 23 Well, I'm sorry. My apologies. I'll take 24 that back. 25 In the context of this memo,</p>	<p style="text-align: right;">Page 189</p> <p>1 Q. Was the concern here also that 2 could not -- that Dr. Ward's lab would not 3 replicate what Dr. Krah's lab was -- 4 A. No. 5 Q. -- coming up with? 6 A. That's not what I said. That is 7 not the concern. The concern is whether the 8 assay could be run with sufficient precision 9 so that one would be able to achieve a data 10 set -- remember, this is a biological assay, 11 biological assays are very difficult to run 12 with appropriate precision. That one would be 13 able to achieve a data set with tight enough 14 confidence intervals that would allow you to 15 address the hypothesis of the 007 study. 16 Q. Have you seen any documents 17 which say that Dr. Ward's lab was not capable 18 of doing that? 19 A. I have not seen any documents, 20 but it is -- the decision is not based on data 21 that would suggest that one is not capable of 22 doing it. The decision is made on the basis 23 of whether or not there are data that show 24 that one is capable of doing it. So the 25 absence of such data and given the time</p>

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<p style="text-align: right;">Page 190</p> <p>1 constraints could very much have led someone 2 to make the decision not to transfer the assay 3 and to keep it internally. 4 Q. Which lab was able to achieve 5 the tight precision at Merck? 6 A. Well, again, it was from, again, 7 reading that memo and Dr. Shaw's notation that 8 the assay was run with the tight set 9 of variant, and it was a validated assay, that 10 we had what appeared to be reasonably good 11 precision around the assay. 12 Q. By keeping it with Dr. Krah's 13 lab, you could ensure that -- what the result 14 was going to be, couldn't you? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: No, you could 17 ensure that the -- 18 MS. DYKSTRA: Misstates his 19 testimony. 20 THE WITNESS: -- assay would run 21 consistently, could run with good 22 accuracy and prescription, and would 23 allow you to generate data that you 24 could then cross compare across the 25 three different arms of the study to</p>	<p style="text-align: right;">Page 192</p> <p>1 A. I don't recall if we actually 2 had a contract or not. 3 Q. If there were such a contract, 4 would that indicate that there was some 5 thought that Dr. Ward's lab was capable of 6 doing the kind of precision you're talking 7 about? 8 A. No, because contracts can be 9 established prospectively with the supposition 10 that, you know, we'll actually execute the 11 contract and actually pay for the work and do 12 the work, you know, if we decide to use the 13 individual. I've done contracts all the time 14 that indicate -- before I determine whether or 15 not I'm actually using somebody. 16 MR. BEGLEITER: Let me show you 17 one document and we'll go to lunch. 18 This is going to be 18. 19 - - - 20 (Exhibit Emini-18, E-mail 21 exchange, 00448867 & 00448868, was 22 marked for identification.) 23 - - - 24 BY MR. BEGLEITER: 25 Q. So your name is not on this?</p>
<p style="text-align: right;">Page 191</p> <p>1 address the hypothesis of the study. 2 It is not to ensure that you would get 3 a specific set of data coming out. 4 BY MR. BEGLEITER: 5 Q. You're saying that Dr. Ward's 6 lab, as far as you can tell from reading this 7 document, was incapable of doing that? 8 MS. DYKSTRA: Objection. Again, 9 misstates testimony. 10 THE WITNESS: No. I did not say 11 that he was incapable of doing it. I 12 said there was uncertainty that it 13 could be done. But by definition, that 14 uncertainty exists not just for 15 Dr. Ward but for every other high 16 level, highly trained virologist on the 17 planet unless you generate active data 18 to show that you can maintain the same 19 accuracy and precision, which it is 20 very difficult across laboratories 21 running biological assays. So it's not 22 specific for Dr. Ward. 23 BY MR. BEGLEITER: 24 Q. Do you know if Merck went so far 25 as to have a contract with Dr. Ward's lab?</p>	<p style="text-align: right;">Page 193</p> <p>1 A. No. Not in the top ones, no. 2 The one at the bottom. 3 Q. It says, I had a long -- the one 4 Alan Shaw to David Krah, I'm going to ask you 5 whether or not this has any recollection to 6 you. Do you recollect this? 7 A. No, I don't. 8 MS. DYKSTRA: Object. Let him 9 read through this. 10 MR. BEGLEITER: Sure. Go ahead. 11 I'm telling him what I'm going to ask 12 him, that's all. 13 MS. DYKSTRA: Understood. 14 BY MR. BEGLEITER: 15 Q. So the date on this e-mail, the 16 second one is November -- September 25, 2000. 17 If you'll recall the dates on the ones that 18 was sent to you on the personal memos that you 19 saw were March 29, 2001. Do you see that? 20 A. Yes. 21 Q. So they're six months? 22 A. Six months roughly. 23 Q. And would you agree, sir, that 24 there were problems in the lab at the end of 25 September 2000?</p>

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<p style="text-align: right;">Page 194</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: Well, what I read 3 in this memo, again, no direct 4 recollection other than what I'm 5 reading here, is that there was -- all 6 of this relates to the fact that we 7 were talking about the potential for 8 hiring additional people power for the 9 laboratory, additional personnel for 10 the laboratory. There was some concern 11 that a hiring freeze was going to be 12 put into place by the company which 13 happened on occasion all the time. And 14 there was a discussion going back and 15 forth on this and I apparently had a 16 discussion with Alan Shaw noting that 17 one of the things that we probably 18 needed to have a careful look at in 19 David Krahn's laboratory was the issue 20 of turnover within the laboratory. 21 BY MR. BEGLEITER: 22 Q. In the third -- the fourth 23 paragraph beginning, "We had a discussion of 24 what the coming workload would be for our 25 group," do you see that sentence?</p>	<p style="text-align: right;">Page 196</p> <p>1 BY MR. BEGLEITER: 2 Q. What do you think he meant by 3 that? 4 A. What he was concerned about was 5 that he was getting frustrated over all the 6 time and effort that was being spent in the 7 laboratory around the mumps assay in support 8 of the 007 study. Because recall the 9 laboratory was originally set up to be a 10 research laboratory. They were working on 11 varicella. There was a strong desire to pick 12 up work on an influenza vaccine program as you 13 can see is indicated here. And that the mumps 14 assay between the work that was required for 15 the development of the assay, to come up with 16 an assay that would be suitable to address the 17 hypothesis in 007 and then obviously was being 18 contemplated at the time transferring the 19 assay to Dick Ward's laboratory so as to 20 alleviate his laboratory and actually having 21 to run the assays was part of the heavy 22 workload that was ongoing in the lab. 23 Q. So there was a capacity problem 24 that was -- 25 A. The same as we were saying</p>
<p style="text-align: right;">Page 195</p> <p>1 A. Yes. 2 Q. And the "we" is you and Dr. Shaw? 3 A. Yes. 4 Q. And "As I see it, the current 5 major things are varicella support for Pharm 6 R&D..." What's that? Do you know what that 7 is? 8 A. That was support of the -- 9 Q. Chicken pox. 10 A. -- pharmaceutical research and 11 developing, this was at the time that the 12 varicella vaccine was being developed so the 13 laboratory was providing the biological 14 support for that work. So that needed to be 15 done. 16 Q. "...which should tail off over 17 the next six to eight months..." 18 Do you see that? 19 A. Yes. Eight months would include 20 March 29th. 21 Q. Transferring this I will say 22 freaking, does that sound right to you? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: Well, I don't 25 know.</p>	<p style="text-align: right;">Page 197</p> <p>1 before. 2 Q. There was a capacity problem at 3 the lab. Go ahead, answer. 4 A. Yes, there was a capacity 5 problem at the lab. My apologies. 6 MR. BEGLEITER: Let's go to 7 lunch. 8 VIDEOGRAPHER: The time is now 9 1:39. 10 - - - 11 (A recess was taken.) 12 - - - 13 VIDEOGRAPHER: The time is now 14 2:36. This begins disc four. 15 BY MR. BEGLEITER: 16 Q. Good afternoon, Doctor. 17 A. Hello. 18 Q. What is an SOP, standard 19 operating procedure? 20 A. Standard operating procedure. 21 Q. What is it in relation to what's 22 in Protocol 007 or one of the other 23 clinical -- 24 A. A standard operating procedure 25 can refer to any one of a number of different</p>

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<p style="text-align: right;">Page 198</p> <p>1 things, but in the context of our ongoing 2 discussion here, it would be a standard 3 operating procedure that describes the 4 procedure for the conduct of a specific assay 5 and how to interpret the data from the assay, 6 how to actually run the assay, how to do it, 7 what you needed to control. 8 Q. Among other things, did it sort 9 of set the rules for the assay? 10 A. It depends what you define by 11 rules. What do you mean by rules? 12 Q. How the assay is to be conducted. 13 A. How the assay is to be 14 conducted. Yes, it is the procedure for 15 operating the assay. 16 - - - 17 (Exhibit Emini-19, 11/13/00 18 E-mail with attachment, 00009013 - 19 00009034, was marked for identification.) 20 - - - 21 BY MR. BEGLEITER: 22 Q. Could we hand Emini-19 to the 23 witness. It's docket number -- Bates-numbered 24 MRK 9013 through 9034. 25 This is a rather long document.</p>	<p style="text-align: right;">Page 200</p> <p>1 Q. Do you have any recollection of 2 the preliminary subset? 3 A. I had no recollection from the 4 time, no, only when reviewing documents. 5 Q. This paragraph indicates that 6 there were approximately 1,980 subjects 7 enrolled. Right? 8 A. Yes. 9 Q. From the subset, this was a 10 randomly selected subset of approximately 600 11 subjects, about 200 per group. Do you see 12 that? 13 A. Right. 14 Q. That doesn't ring a bell? 15 A. Other than what it says, no. 16 Q. It says, "Merck is still blinded 17 to the treatment assignments." Is that -- 18 A. Well, that's what normally would 19 we do when you do a subset analysis so you 20 don't suffer a statistical penalty. 21 Q. So in other words, when subset 22 or the whole thing, blinding is required? 23 A. So when you do a subset 24 analysis, prior to having -- prior to having 25 analyzed the data to address the primary</p>
<p style="text-align: right;">Page 199</p> <p>1 I'll just tell you you can read as much as you 2 want, I'm not stopping you, but I'll be 3 talking about the first page, 9013. I'll be 4 asking you questions about that, and 9022. 5 Aside from that, I'm not going to ask any 6 questions. Well, that's not true. And also 7 page 9017. Those are the only three pages I'm 8 going to be making reference to. 9 A. Okay. 10 Q. So looking at the first page, 11 9013, did you receive this document, including 12 the attachments, during the regular course of 13 your employment? 14 A. It was addressed to me as one of 15 the recipients of the e-mail. So yes, I did. 16 Q. It was received on November 13, 17 2000? 18 A. November 13, 2000. 19 Q. Great. Now, if you can turn to 20 page 9022. I'll ask you to read, you can read 21 it to yourself if you wish, a "Preliminary 22 Subset Analysis." The first paragraph and 23 then I'm going to ask you some questions about 24 the preliminary subset. 25 A. Okay.</p>	<p style="text-align: right;">Page 201</p> <p>1 endpoints of the study, right, so typically 2 you would do this because this is a specific 3 immediate question that needs to be addressed, 4 as was the case here apparently, then you 5 could do such a subset analysis. But what was 6 very critically important was to maintain the 7 blind of the study so that the statistician 8 and the other personnel involved in generating 9 the data, not involved in actually analyzing 10 the data for the final endpoints of the study, 11 are blinded to the treatment assignments. 12 Standard procedure. 13 Q. A statistician in this case was 14 not blinded -- was unblinded. You can't blind 15 a statistician. Right? 16 A. No, you unblinded the statistician 17 to do the subset analysis, but that would not 18 the same statistician that did do the final 19 analysis. The final analysis statistician 20 would remain blinded. 21 Q. The sentence at the end of -- 22 what is a treatment assignment? 23 A. The treatment assignment is 24 related to the three groups of the study. 25 Remember there are four potency levels --</p>

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<p style="text-align: right;">Page 202</p> <p>1 excuse me, three potency levels? 2 Q. 4.9, 4.0, 3.7, is that what you 3 said? 4 A. Yes. 5 Q. And then at the end it says 6 regardless of -- the end of the paragraph that 7 begins the statistician not associated with 8 the conduct of the trial. In that paragraph 9 it says, regardless of the outcome of the 10 preliminary analysis, the sera from the remain 11 set will be tested in a blinded fashion and 12 all subject will be included in the final 13 analysis. 14 A. That's correct. 15 Q. That's looking forward beyond 16 the preliminary subset into the final -- into 17 the completion of the assay? 18 A. Yes. 19 Q. Now, do you recall, looking at 20 the document, what the day of the unannounced 21 inspection we talked about before? I could 22 remind you but maybe you remember. Do you 23 remember the inspection that resulted in the 24 483? 25 A. Resulted in 483, yes.</p>	<p style="text-align: right;">Page 204</p> <p>1 Q. Yes. 2 A. No. The inspector came in the 3 morning as being the senior person related to 4 the area that she wanted to assess. I was 5 handed what is known as a Form 482, which is 6 the announcement of the inspection. And then 7 we made sure that we pulled together the 8 people who needed to be pulled together and 9 informed regulatory. Regulatory is 10 responsible for interacting with the inspector 11 during the inspection. I retired and was not 12 called back until the inspection had been 13 completed and the 483 had been prepared. To 14 my recollection, of course. 15 MR. BEGLEITER: Have this 16 marked, please, as Number 20, I guess. 17 Let me just announce it. This is a 18 document Merck 8835 through 8839. It's 19 a four-page document, if you could mark 20 it. 21 - - - 22 (Exhibit Emini-20, E-mail 23 string, 00008835 - 00008839, was marked 24 for identification.) 25 - - -</p>
<p style="text-align: right;">Page 203</p> <p>1 Q. You want to look at that just -- 2 you can fix the date, that's important. 3 A. I have to dig through here. Do 4 you remember which one it was? 5 MS. DYKSTRA: Look at Exhibit 8. 6 THE WITNESS: Exhibit 8. There 7 was one that actually had the 483 in 8 it. 9 BY MR. BEGLEITER: 10 Q. On the second page? 11 A. That's the one you're referring 12 to. That's the second page. 13 Q. The handwritten 483. 14 A. That would be 7. 7, yes. 15 Q. I'm asking you to look at it to 16 confirm the date. 17 A. Confirm the date? 18 Q. Of the inspection. 19 A. That would have been August 6, 20 2001. 21 Q. At the time of the inspection 22 going on, was anybody giving you any updates 23 as to what was going on, anybody reporting to 24 you on the inspection on that date on the 6th? 25 A. On the date of the inspection?</p>	<p style="text-align: right;">Page 205</p> <p>1 BY MR. BEGLEITER: 2 Q. My focus will be on your e-mail 3 of August 7th, but you can read the whole 4 thing. The first e-mail in the string. 5 A. Okay. 6 Q. And going to that -- did you -- 7 are you the author of some of these e-mails? 8 A. Yes, I am. 9 Q. Did you receive all of them as 10 part of your usual -- 11 A. Let me see. Let me just check 12 it to see. 13 Q. Take your time. 14 A. Yes, I either wrote or received. 15 Q. Going to the first e-mail, I see 16 this is to Anthony Ford-Hutchinson and Peter 17 Kim. 18 A. Yes. 19 Q. With cc's to various people. 20 These people, Hutchinson and Kim, I think you 21 answered this morning you weren't sure who was 22 there, whether they were both your report -- 23 the person to whom you reported at the same 24 time? 25 A. So according to this note Peter</p>

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1 Kim was obviously there in the company since
 2 they sent him the message as well. So I would
 3 have been reporting to Tony Ford-Hutchinson
 4 who was, in turn, reporting to Peter Kim.
 5 Q. Peter Kim was above him?
 6 A. Was above him. And then, in
 7 turn, Peter Kim at that point since Ed
 8 Scolnick was still there, he had not yet
 9 retired, was reporting to Ed Scolnick.
 10 Q. Who was the president?
 11 A. Who was the president of the
 12 research laboratory, and Peter Kim eventually
 13 became president of the research laboratory
 14 when Ed Scolnick retired.
 15 Q. What was your purpose in writing
 16 this e-mail, if you can recall?
 17 A. The purpose in writing the
 18 e-mail is as noted in the e-mail, we had
 19 received a Form 483 with inspection
 20 observations from the FDA, and I felt it
 21 appropriate to write a note to my supervisors
 22 indicating the four observations as were noted
 23 in the e-mail that the inspector had made on
 24 the Form 483. And to note to my opinion of
 25 the nature of those observations and what we

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1 were at least at that time contemplating to do
 2 subsequently. This was the day after the
 3 inspection.
 4 Q. And just some abbreviations
 5 here. GMP is?
 6 A. So GMP stands for good
 7 manufacturing -- formerly stands for good
 8 manufacturing practices. The terminology is
 9 also used generally to refer, at least at the
 10 time, to refer to appropriate defined
 11 procedures for conducts of -- for anything
 12 related to a potential product. So the term
 13 was used very generally, GMP. These days the
 14 term is much better defined.
 15 Q. In the last paragraph you talk
 16 about the correlation being excellent between
 17 something and ELISA. Is the something the
 18 PRN?
 19 A. The neut assay results and I
 20 presume that this was referring to the PRN,
 21 right, which was being run at the time.
 22 Q. Was correlation something that
 23 was important to the FDA?
 24 MS. DYKSTRA: Objection. Form.
 25 THE WITNESS: Correlation was a

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1 note -- well, there was --
 2 BY MR. BEGLEITER:
 3 Q. Your counsel is right, that
 4 wasn't a good question.
 5 A. I know. Try it again.
 6 Q. Is it your understanding that
 7 the correlation was important to the FDA?
 8 MS. DYKSTRA: Objection. Form.
 9 THE WITNESS: Correlation was
 10 important only insofar as these were
 11 two independent measures of an immune
 12 response to the vaccine. If we were to
 13 use both sets of data in order to
 14 compare the three different dose levels
 15 of the vaccine in 007, then a general
 16 correlation, didn't have to be perfect,
 17 but a general correlation would fall
 18 into the category of nice to have.
 19 BY MR. BEGLEITER:
 20 Q. It wasn't a correlation between
 21 the neutralization in assay --
 22 A. And the ELISA.
 23 Q. -- and the ELISA was not
 24 required?
 25 A. It depends on what you mean by

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1 "correlation." It is an exact correlation?
 2 Q. Well, you wrote the e-mail.
 3 What did you mean?
 4 A. So what I meant by "correlation"
 5 would be that in general if you're looking at
 6 a population of samples, right, not individual
 7 one-to-one samples, but you're looking at a
 8 population of samples, if the neutralization
 9 assay showed, let's say, 89 percent
 10 seroconversion, plus or minus a certain
 11 variance, that the ELISA looking at the same
 12 population of samples would also show within
 13 that variance an 89 percent seroconversion
 14 within the variance established by the assay.
 15 Q. Why did you inform the
 16 supervisors that you're writing this e-mail to
 17 of that fact?
 18 A. Well, because the question that
 19 this one was referring to was observation or
 20 what I was referring to as violation number
 21 one. Or which related to, and we can read it
 22 here, in that it potentially, that observation
 23 by the inspector potentially suggested that
 24 there might be an issue with the validity of
 25 the data because there had been changes that

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1 were made to the spreadsheet that contained
 2 the data but without noting the reason why the
 3 change was made. That was the basis of the
 4 observation. So, therefore, that
 5 automatically raises the issue to say are we
 6 certain that the data as they currently exist,
 7 or the data as they were originally derived,
 8 are they, in fact, reflecting the same
 9 conclusion. That's the observation.
 10 So, therefore, the resulting
 11 data, what we did is that we took the data, we
 12 submitted it to the clinical statistical --
 13 I'm reading directly from the memo.
 14 Correlated the neut assay results with that of
 15 an independently performed ELISA. The ELISA
 16 was being performed independently. And as a
 17 result, I noted that the correlation was
 18 excellent suggesting that there were no global
 19 problems. In other words, if changes were
 20 being made to the original data set that
 21 radically changed the conclusion of that data
 22 set, it might have a certain likelihood of
 23 showing a miscorrelation with the
 24 independently performed ELISA. So this was
 25 simply an initial indication of comfort taken

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1 that there wasn't a global issue with the
 2 data. It was not to say that what was done
 3 was correct. It just that it was not a global
 4 issue with the data.
 5 Q. The ELISA test, the ELISA test
 6 and the neutralization assay, the ELISA assay
 7 and neutralization assay, they're different
 8 assays. Right?
 9 A. Completely different assays.
 10 Q. It also says it should be
 11 noted -- this in the last paragraph on page
 12 839, "It should be noted that all samples were
 13 tested, per protocol, with the lab personnel
 14 blinded to sample identification."
 15 A. That is correct.
 16 Q. What does that mean?
 17 A. That means that the lab
 18 personnel did not know whether or not the
 19 sample came from our number one or number two
 20 or number three. In other words, it did not
 21 know where the serum sample was taken and
 22 whether it was -- and which of the three dose
 23 levels of the vaccine that the individual from
 24 whom the sample was taken was inoculated with.
 25 Q. Is that blinding important as

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1 far as you're concerned?
 2 A. The blinding is essential in
 3 order to be able to do that, right, because it
 4 is intended to avoid bias on the part of the
 5 operator.
 6 Q. If you go to the next e-mail,
 7 the one above it, also signed by you, you
 8 say -- and what you say at the end is "The
 9 points in this note will be captured by Alan
 10 Shaw in the draft of the responses of each of
 11 the individual notices of violation."
 12 A. Yes.
 13 Q. Do you see that?
 14 A. Yes.
 15 Q. That's, again, you're referring
 16 to 483 there?
 17 A. Yes, the four individual points
 18 made in 483.
 19 Q. You can read it if you want, but
 20 the point is that Alan Shaw was going to
 21 respond?
 22 A. Alan Shaw was going to work on
 23 making a draft of the responses. Who
 24 ultimately responded formally? Probably it
 25 either came -- in this case it either came

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1 from me or it came from someone in regulatory
 2 in terms of the formal response. But the
 3 draft was being put together by Dr. Shaw.
 4 Q. I notice something in the
 5 original message.
 6 A. Which one?
 7 Q. The one at the bottom of 838 was
 8 not sent to Dr. Shaw.
 9 A. No, this was a message that was
 10 sent directly by me to my management.
 11 Q. The e-mail we were just talking
 12 about where he says he's going to capture the
 13 points was also not sent to Dr. Shaw.
 14 A. Okay.
 15 Q. As a matter of fact, none of
 16 these e-mails were sent, except for one.
 17 A. Except the reply that came back
 18 from regulatory.
 19 Q. Except for Dr. Ukwu?
 20 A. Ukwu, right.
 21 Q. Let's get to that. Okay. So
 22 weren't you talking to Dr. Shaw on the day of
 23 the inspection and the day after the
 24 inspection, the days you were --
 25 A. Certainly the day after --

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<p style="text-align: right;">Page 214</p> <p>1 MS. DYKSTRA: Let him finish. 2 BY MR. BEGLEITER: 3 Q. Were you talking to Dr. Shaw on 4 the date of the inspection and the day after 5 and then after that? 6 A. I do not recollect directly, but 7 I am certain based upon what we see here that 8 I was obviously in conversation with Dr. Shaw 9 certainly the day after. And depending upon 10 when the inspector left, I don't know if we 11 conferred that afternoon of the inspection. 12 Q. Everything you wrote in these 13 two e-mails you believed to be true? 14 A. Yes. 15 Q. Do you still believe them to be 16 true? 17 A. Based on what I see here, yes. 18 Q. Well, based on anything. Do you 19 still believe them to be true? 20 A. Certainly I believe -- yes, I 21 believe them to be true. I have no evidence 22 to the contrary that they're not true. 23 Q. Okay. You also didn't send any 24 of these e-mails to Dr. KraH. Isn't that 25 right?</p>	<p style="text-align: right;">Page 216</p> <p>1 Q. No, no. You can recall that you 2 spoke to somebody but not remember what you 3 said. 4 A. I know, but what I said, my 5 answer -- my apologies. My answer to your 6 question is, I have no recollection of a 7 discussion, per se. 8 Q. Why not? 9 MS. DYKSTRA: Objection. 10 THE WITNESS: Because I don't 11 have one. 12 BY MR. BEGLEITER: 13 Q. No, no, no. Why don't you 14 have -- well, you're saying you could have had 15 a discussion with Dr. KraH but you just don't 16 remember? 17 A. Well, yes, I could have had a 18 discussion with Dr. KraH, but I just don't 19 remember. Yes. I literally don't remember. 20 Q. Okay. Now, take a look at Alan 21 Shaw's e-mail of August 8, 2001, at 9:36 p.m. 22 A. Which one is this? 23 Q. That's the cover page. 24 A. The cover page? 25 Q. The first page, 8835. The</p>
<p style="text-align: right;">Page 215</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: These are e-mails 3 that were intended for my immediate 4 management. 5 BY MR. BEGLEITER: 6 Q. I understand that. But it was 7 Dr. KraH's lab was the one that was inspected. 8 I'm not saying you should have, I'm just 9 saying the fact is you didn't send -- 10 A. I didn't send them, no. 11 Q. Okay. Fine. 12 A. No. 13 Q. Okay. And did you discuss with 14 Dr. KraH in the days after, the day of and the 15 days two or three days after the inspection 16 what happened in the inspection? 17 A. I have no recollection of the 18 actual discussions themselves. 19 Q. But did you recall actually 20 speaking with him? 21 A. I have no recollection of the 22 actual discussions themselves. So by 23 definition, I don't have a recollection of 24 actually having spoken with him. Maybe we're 25 saying the same thing.</p>	<p style="text-align: right;">Page 217</p> <p>1 bottom one on that page. 2 A. Yeah. 3 Q. He suggests, "I would suggest 4 that people from your group..." meaning 5 Henrietta Ukwu's group. Right? "...plus Kati 6 Abraham fix a time with Dave KraH and Mary 7 Yagodich to make your audit." 8 A. Right. 9 Q. What audit are you talking 10 about? 11 A. So, again, in reviewing the 12 multiple back and forth communications that 13 occurred with the agency after this initial 14 inspection in the subsequent months, what 15 clearly we conducted and then asked for was a 16 general audit. First of all, there were 17 audits related to ensuring that what had been 18 observed by the inspector in the case of 19 Dr. KraH's laboratory would result in -- first 20 of all, would not result in any change to the 21 interpretation of the data. That was 22 fundamentally critical, so we conducted that 23 assessment. We then also, you recall that 24 some of these observations were observations 25 related to operations in terms of how things</p>

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<p style="text-align: right;">Page 218</p> <p>1 were operating in the laboratory. So we 2 conducted an audit to make certain that if 3 those operations were, in fact, not being 4 conducted the way in which the inspector noted 5 to us, that we would take appropriate 6 corrective action to make sure that that was 7 the case. And on top of all of that, we also 8 went on in addition to looking specifically at 9 Dr. Krahs laboratory, we also took the 10 opportunity to conduct a broader audit across 11 all activities that were associated within the 12 organization that ran under standard operating 13 procedures to make sure the standard operating 14 procedures were in place and that activities 15 would be followed according to the appropriate 16 standard operating procedures. Not an unusual 17 set of activities. 18 Q. That resulted in the August 20th 19 letter which number I don't have. 20 A. Which one is this now? 21 MS. DYKSTRA: Exhibit 8. 22 BY MR. BEGLEITER: 23 Q. Exhibit 8. 24 A. Take a look to be certain. This 25 was the initial response, if I remember</p>	<p style="text-align: right;">Page 220</p> <p>1 recollection. Let's have a look. 2 MR. BEGLEITER: I'd like to have 3 marked for identification Merck 52243. 4 It's a one page e-mail. 5 - - - 6 (Exhibit Emini-21, 8/9/01 7 E-mail, 00052243, was marked for 8 identification.) 9 - - - 10 BY MR. BEGLEITER: 11 Q. If you can read -- I'm only 12 going to ask you about paragraph 1. You can 13 read anything you want to read. 14 A. This does not refer to sample 15 blinding. This refers to the blinding of the 16 counting of the plaques on the plate. It's a 17 different situation than the one you were 18 talking about. 19 Q. Well, was it appropriate for 20 someone to be unblinded, for the head of the 21 lab to be unblinded? 22 A. For counter-qualification, yes, 23 that's perfectly acceptable. 24 Q. Is that anywhere in the SOP? 25 A. I don't recall if it was</p>
<p style="text-align: right;">Page 219</p> <p>1 correctly. Yes, it was. This was the initial 2 response to the agency that I responded to 3 that addressed what we had done to reply to 4 the observations that were made by the 5 inspector. 6 Q. So were you under the impression 7 when you wrote that letter -- 8 A. Sorry, which letter, Number 8? 9 Q. Number 8. 10 A. Yes. 11 Q. -- that the Protocol 007 had 12 been a blinded protocol except for the 13 statistician? 14 A. That 007 had been a blinded 15 protocol. Well, by definition it had been 16 completely blinded. The only thing that was 17 looked at, there was no indication whatsoever 18 that the laboratory staff had any opportunity 19 to unblind the samples. 20 Q. Do you know sitting here today 21 that Dr. Krahs himself was unblinded? 22 MS. DYKSTRA: Objection. 23 MR. BEGLEITER: I'm asking if he 24 knows that, I'm not saying it's true. 25 THE WITNESS: I have no</p>	<p style="text-align: right;">Page 221</p> <p>1 specifically in the SOP, but typically someone 2 needs to be unblinded for a qualification to 3 be appropriately conducted. The individuals 4 who were blinded were the individuals who were 5 looking -- that were actually running the 6 counters with the individual samples. 7 Remember what the counters are doing, that 8 this is individual counting of the plaques on 9 the assay. So they were blinded to each 10 other's results. He knew which ones were the 11 actual value numbers because he was using, as 12 he notes here very clearly, "...the workbook 13 printout as a guide to check for 14 extravariable/single dilution positive 15 samples." 16 So basically they would be -- so 17 he was aware what the numbers were and then 18 essentially asking you count them, you count 19 them, you count them, and he was assessing 20 based upon what the original numbers were, the 21 variation that occurred if you counted them or 22 you counted them or you counted them. 23 Q. The plates he was talking about 24 were the plates that actually where the assay 25 was conducted. Is that right?</p>

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<p style="text-align: right;">Page 222</p> <p>1 A. This would be the plates in 2 which the assay was conducted, yes. 3 Q. And his knowing what those 4 plates showed in terms of plaques, that 5 wouldn't bias him? 6 A. No. 7 MS. DYKSTRA: Objection. 8 THE WITNESS: It depends on what 9 he was doing. In this particular case 10 he was doing counter-qualification. So 11 there is no bias associated with that. 12 This was so that he could conduct an 13 independent assessment of the 14 variability that was occurring among 15 three different potential readers. 16 Probably as a result of, you know, 17 having taken a careful look again to 18 determine what the variability of the 19 counting procedure was. 20 BY MR. BEGLEITER: 21 Q. Did you inform supervisors who 22 you sent your e-mails to on the 7th and 8th 23 that, in fact, that Dr. Krah had been 24 unblinded on the counter-qualifications? 25 A. No, because it was not relevant</p>	<p style="text-align: right;">Page 224</p> <p>1 Q. I didn't -- I asked a question 2 about blinding. I'm saying there was a 3 workbook printout. 4 A. Yes. 5 Q. As a guide to check extra 6 variables/single dilution positive samples? 7 A. Right. 8 Q. So in other words, Dr. Krah knew 9 what the single -- where the single -- which 10 ones were in single dilution positive samples. 11 Is that right? 12 A. Right. 13 Q. And that could tell him whether 14 or not they were pre-positives or not. Isn't 15 that right? 16 A. No. I don't see how that would 17 be possible. 18 Q. You mean having a printout that 19 tells you what each plate, what the plates -- 20 A. It does not identify the sample. 21 It's simply says these are the numbers that 22 were counted. It does not identify from whom 23 or from which individual the sample came from. 24 That was information that would only be 25 available to the blinded statistician. The</p>
<p style="text-align: right;">Page 223</p> <p>1 to the overall inspection issue. 2 Q. Well, did you -- you had 3 represented to your supervisors that, in fact, 4 there had been blinding? 5 A. Yes. 6 Q. Now, could the blinding, since 7 Dr. Krah would know the pre-positives, 8 post-positives, pre-negatives, would know 9 that -- would know who was what, wouldn't 10 that -- couldn't that bias the taker of the 11 test? 12 A. No, it says here, if I read this 13 correctly, it says, "...we are blinded for our 14 counter qualification...for the rechecks of 15 the current assays that I have done. I have 16 not been blinded since I was using the 17 workbook printout as a guide to check for 18 extravariable/single dilution positive 19 samples." So he was checking to see if there 20 were extra variable/single dilution positive 21 samples, the values that were being generated 22 were the blinded values being -- were the 23 values that were being blindly assessed by 24 the blinded counters. He was not changing any 25 numbers there himself.</p>	<p style="text-align: right;">Page 225</p> <p>1 samples are blinded by code. 2 Q. Then explain this to me. For 3 the majority of the plates, the pen marks were 4 left on the plate for initial recheck to see 5 if plaques were over or undercounted, i.e., 6 each pen mark -- was each pen mark associated 7 with an identified plaque? 8 A. Right. 9 Q. And if there was a difference 10 noted, the spots were removed and the plate 11 was recounted. 12 A. Right. 13 Q. Is that appropriate to do, to 14 remove the spots? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: If you don't 17 remove the spots, you can't recount 18 because you won't be able to see the 19 plaques so you have to remove the 20 spots. 21 BY MR. BEGLEITER: 22 Q. Who asked them to recount? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: I don't recall who 25 specifically asked to do the</p>

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<p style="text-align: right;">Page 226</p> <p>1 recounting. I don't recall who 2 specifically asked. I can tell you -- 3 BY MR. BEGLEITER: 4 Q. I take it from that that you 5 have no recollection of asking him? 6 A. I have no recollection of asking 7 him personally to do the recount. 8 Q. You have no recollection of 9 discussing with Dr. Shaw either? 10 A. I have no direct recollection of 11 discussing it with Dr. Shaw. But this would 12 have been part of the procedure to assess the 13 quality of the data. 14 Q. Shouldn't the fact that there 15 was a recheck going on be something that 16 Dr. Shaw should have known? 17 MS. DYKSTRA: Objection. 18 THE WITNESS: He may very well 19 have known and probably did know it. I 20 just don't recall ever having -- 21 20 years later having the conversation 22 with him. 23 BY MR. BEGLEITER: 24 Q. But it wasn't important enough 25 to write an e-mail to you to tell you that it</p>	<p style="text-align: right;">Page 228</p> <p>1 communications, so there were discussions that 2 were ongoing as normally would be the case 3 between regulatory and CBER as a result of the 4 inspection. And part of the effort probably 5 involved, based upon what I read here, a 6 rechecking of the data and the actual counts 7 that were done to determine if there was a 8 complete -- if there was an issue in terms of 9 following the SOP and if the numbers which had 10 been changed without explanation in that 11 original spreadsheet, if one does it again, 12 does one come up with the same set of 13 conclusions. 14 Q. In Exhibit 7, which is the 483, 15 contains the 483, number 1 we already read, 16 raw data is being changed with no justification. 17 A. Right. 18 Q. For example. Okay. 19 A. No justification may mean that 20 no justification was noted on the document, 21 not that there was no justification. Big 22 difference. 23 Q. And then two days later, three 24 days later, August 9th, Dr. Krah says that he 25 was unblinded as to counter-qualifications.</p>
<p style="text-align: right;">Page 227</p> <p>1 was going on. Is that what you're saying? 2 MS. DYKSTRA: Objection. 3 Mischaracterizes his testimony. 4 THE WITNESS: No. He just -- 5 first of all, I don't recall if he did 6 write me an e-mail because we haven't 7 reviewed every single e-mail that went 8 back and forth between myself and 9 Dr. Shaw. But this activity was going 10 on. It was undoubtedly part of the 11 operational audit and reassessment of 12 the data since it was questioned in 13 terms of how the original data were 14 generated or at least how they were 15 recorded, not necessarily generated but 16 how they were recorded. That's 17 perfectly standard. 18 BY MR. BEGLEITER: 19 Q. Was CBER told about the 20 rechecking -- 21 MS. DYKSTRA: Objection. 22 BY MR. BEGLEITER: 23 Q. -- by you? 24 A. Not by me directly. My 25 communications with CBER were formal</p>	<p style="text-align: right;">Page 229</p> <p>1 Do you think that something -- withdrawn. 2 Did you believe this was 3 something that should have been told to the 4 FDA? 5 A. No. Because they're not 6 correlated with each other. He was doing a 7 counter-qualification which was to ascertain, 8 since they were going to recount the plates 9 and the plates were apparently being recounted 10 by multiple individuals, so you go through 11 this qualification process to see -- because 12 remember, these are manual counts. They rely 13 on human judgment. So, therefore, if analyst 14 number one did it and analyst number two and 15 analyst number three, and they, according to 16 the memo, were all blinded to each other in 17 terms of what they were actually counting, in 18 other words, analyst number two was not 19 looking over the shoulder of analyst number 20 one. Everything was done blindly. So analyst 21 number one would do a set of counts, analyst 22 number two would do a set of counts and 23 analyst number three would do a set of counts. 24 They would sit there, okay, and then a third 25 party, presumably a statistician, would sit</p>

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<p style="text-align: right;">Page 230</p> <p>1 down, look across the counts and determine, 2 okay, so what are the actual counts and how 3 close are they in their actual counts. Now, 4 when one does that, there is sometimes -- and 5 this is a qualification effort that was 6 ongoing, so these are qualifications. 7 Remember, this is like a validation. It's to 8 determine whether or not your eyes count X 9 number of plaques to my eyes also count X 10 number of plaques, if there is a big 11 difference between what you count and I count, 12 then we have an issue here. Whose numbers do 13 we believe? Do we believe your numbers. Do 14 we believe my numbers. So, therefore, it 15 requires at that point to sit down, do some 16 training, do some assessments so as to 17 coordinate, if you will, how you interpret 18 what you see and how I interpret what I see. 19 You can only do that if then there's another 20 party that really looks to see are there large 21 variabilities. And that apparently is what 22 Dr. KraH was doing. So what he's referring to 23 is the blinding of the -- blinded to the 24 actual plate counting that was going on. This 25 is not blinded -- blinding related to the</p>	<p style="text-align: right;">Page 232</p> <p>1 unintended bias. 2 BY MR. BEGLEITER: 3 Q. What is done to avoid unintended 4 bias? 5 A. The blinding. The blinding is 6 done to avoid unintended bias. 7 Q. And do you know sitting here 8 today whether or not Dr. KraH had access to 9 the pre-positive samples? 10 MS. DYKSTRA: Objection. 11 BY MR. BEGLEITER: 12 Q. Access to know which samples 13 were pre-positive, I should say. 14 A. One -- pre-positive. 15 Q. Yes. 16 A. Please define pre-positive. 17 Q. You don't know what it means? 18 A. No, I think I know what you're 19 asking, but I'm not certain, so I'm asking you 20 to be more precise, please. 21 Q. I'll ask it a different way 22 rather than get into an argument. 23 What Dr. KraH was doing would 24 allow him to know what the count was, what the 25 plaque count was per child. Isn't that right?</p>
<p style="text-align: right;">Page 231</p> <p>1 designation of the actual samples being 2 tested. 3 Q. Could you tell from the counting 4 sheets which pre or post samples were 5 associated with the specific trial? 6 MS. DYKSTRA: Objection. 7 THE WITNESS: Well, by 8 definition -- so one could make the 9 assumption that if, in fact, there was 10 a high degree of neutralization, 11 chances are that this was an immunized 12 individual. But remember they're all 13 immunized individuals in this trial. 14 These children received different 15 potency levels of the vaccine. They 16 were largely immunized. So, therefore, 17 if you're blinded to which group the 18 sample came from, it will have no 19 impact on the final outcome of the 20 trial because that's something that's 21 going to be assessed by the unblinded 22 statistician at the end of the study. 23 Then associates a given value with a 24 given sample from a given arm of the 25 trial. This is done to avoid</p>	<p style="text-align: right;">Page 233</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: That would not 3 allow -- this would not allow him to 4 know that, no. 5 BY MR. BEGLEITER: 6 Q. If he had a notebook that had 7 that information, he would already have known 8 it. Correct? 9 MS. DYKSTRA: Objection. 10 THE WITNESS: Only if the 11 workbook contained the actual 12 designation of the sample and where it 13 came from. The actual designation of 14 the subject to the sample. 15 BY MR. BEGLEITER: 16 Q. Have you ever seen the workbook? 17 A. I have not seen -- I don't -- 18 well, no, I can't answer. I don't recollect 19 having seen this workbook or not having seen 20 the workbook. I do not. 21 Q. Now, sometime before the 22 unannounced inspection, you had spoken to 23 Mr. KraHling? We discussed this already 24 today. You had a conversation with him. 25 A. Right before the unannounced</p>

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<p style="text-align: right;">Page 234</p> <p>1 inspection, yes. 2 Q. Somewhat fairly close to the 3 unannounced inspection. Right? 4 A. Yes. 5 Q. Didn't he tell you that there 6 were -- what did he tell you about the way the 7 counts were being done in the lab? 8 MS. DYKSTRA: Objection. 9 THE WITNESS: So the only 10 recollection I have of that, right, was 11 a notation in a document that I saw 12 over the last few days, right, that 13 indicated that Mr. Krahlung had shown 14 me -- had shown me data suggesting that 15 there were changes being made to the 16 data, pretty much essentially what the 17 inspector noted in the 483 report. 18 That is the best of my recollection. 19 BY MR. BEGLEITER: 20 Q. What document was that? 21 A. So this was a document, if I 22 recall correctly, that was a document, it was 23 an e-mail largely redacted but with a 24 handwritten notation. 25 Q. What did the handwritten</p>	<p style="text-align: right;">Page 236</p> <p>1 might have been some inappropriate changing of 2 data in Dr. Krah's lab? 3 A. The possibility always exists 4 and when someone comes to me, and this has 5 been consistently true of anything I've always 6 done, comes to me with a -- we'll call it an 7 allegation that there might be something which 8 is improper, then one typically refers this to 9 an independent third party to do the 10 assessment. What I can tell you and will tell 11 you is that I did refer this to legal counsel 12 in the company. 13 Q. Did you consider removing 14 Dr. Krah even temporarily from the laboratory? 15 A. There was a -- I don't recall my 16 thoughts at the time but there would have been 17 no reason to do so until the third-party 18 investigation would have been completed. Also 19 what I didn't recall, I really don't recall at 20 the time is whether or not there were actually 21 activities still going on at the time. In 22 other words, additional assays going on at the 23 time. If there had been none going on, then 24 we would have stayed at status quo, stopped 25 everything and just waited for the independent</p>
<p style="text-align: right;">Page 235</p> <p>1 notation say, if you recollect? 2 A. This was somebody who had 3 written to me or made a note of the fact that 4 Mr. Krahlung had shown me some data. I don't 5 recollect the exact terminology. 6 Q. And who did Mr. Krahlung accuse 7 of changing the data? 8 MS. DYKSTRA: Objection. 9 THE WITNESS: I do not recollect 10 the details of the conversation. 11 BY MR. BEGLEITER: 12 Q. Didn't Mr. Krahlung accuse -- 13 withdrawn. 14 Did Mr. Krahlung make the 15 accusation that the changing of data was done 16 in Dr. Krah's lab? 17 MS. DYKSTRA: Objection. Asked 18 and answered. 19 THE WITNESS: I don't recall the 20 details of the conversation. 21 BY MR. BEGLEITER: 22 Q. By the time you received the 23 483 -- by the time you read the 483 and 24 thought about it and did your e-mail the next 25 day, did you consider the fact that there</p>	<p style="text-align: right;">Page 237</p> <p>1 assessment to be completed. 2 Q. Would that have been an 3 appropriate thing to do? 4 MS. DYKSTRA: Objection. 5 THE WITNESS: That would 6 normally being the appropriate thing to 7 do. 8 BY MR. BEGLEITER: 9 Q. You don't recall if that was 10 done or not? 11 A. Well, what did occur -- what did 12 occur was immediately thereafter, as it turned 13 out, the inspector showed up, was within a few 14 days, the 483 was issued, the point was made 15 directly on the 483. Therefore, what we 16 normally would have done independently of that 17 anyway was just went on in response to this 18 case, to the 483. 19 Q. You didn't directly ask Dr. Krah 20 about the allegation -- 21 MS. DYKSTRA: Objection. 22 BY MR. BEGLEITER: 23 Q. -- changing the date? 24 A. I am certain that we may have 25 had some conversation related to it, but</p>

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<p style="text-align: right;">Page 238</p> <p>1 normally once this is referred to a third 2 party for assessment, you allow the third 3 party to conduct their assessment 4 independently of any interaction with the 5 third party because it would not have been 6 appropriate. 7 Q. Was Dr. Krah ever asked by 8 you -- who is the third party you're talking 9 about here? Would that have been legal 10 counsel? 11 A. So the -- it was legal counsel 12 and -- may I? And then I had my -- 13 MS. DYKSTRA: Just legal 14 counsel. 15 THE WITNESS: Just legal 16 counsel. We'll leave it at that. 17 MS. DYKSTRA: Stop at that for 18 privilege issues. 19 THE WITNESS: Privilege issues. 20 BY MR. BEGLEITER: 21 Q. The very last sentence in that 22 paragraph, let me read -- there's two 23 sentences. 24 A. Please. 25 Q. "For the majority of the plates,</p>	<p style="text-align: right;">Page 240</p> <p>1 happens, particularly when one is using human 2 judgment to count plaques, if you count it 3 multiple times, you're going to get 4 potentially multiply different sets of 5 numbers. So that may, as he noted, introduce 6 a bias. But as he noted from a statistical 7 perspective, at least by eye, there were as 8 many increases in numbers as there were 9 decreases in numbers. So when one does a 10 statistical assessment in the end, it will 11 come out in the wash. 12 Q. And Dr. Krah to this very day 13 never told you about this rechecking? 14 MS. DYKSTRA: Objection. 15 BY MR. BEGLEITER: 16 Q. Is that your testimony? 17 A. No, my testimony is I don't 18 recollect having a discussion with Dr. Krah. 19 Q. If there is even a possibility 20 of introducing a bias, do you believe that the 21 FDA should have been informed of that 22 possibility? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: The FDA would 25 automatically have been informed when</p>
<p style="text-align: right;">Page 239</p> <p>1 the pen marks were left on the plate for an 2 initial recheck to see if plaques were over or 3 under-counted (i.e., was each pen mark 4 associated with an identified plaque)..." 5 A. Right. 6 Q. ...and if there was a difference 7 noted, the spots were removed from the -- 8 removed and the plate was recounted. Do you 9 see that? 10 A. Yes. 11 Q. In the next sentence Dr. Krah 12 says something. "This may introduce a bias, 13 but the changes have been both up and down 14 (although largely up due to missed counts)," 15 the last word is in the parentheses. 16 What do you understand him by 17 saying that "this may introduce a bias"? 18 A. Well, by statistical definition, 19 every time you count something more than once, 20 there's a certain probability that you will 21 introduce a bias. And that the criteria 22 that's used for counting the first time, and 23 even in one's own head, can be very different 24 than the criteria that was done the second 25 time. So what then -- so then typically what</p>	<p style="text-align: right;">Page 241</p> <p>1 they looked at the reanalysis in 2 comparison with the initial assessment, 3 because the statistical assessment 4 would have indicated the presence of a 5 statistical bias. So that happens 6 automatically. 7 BY MR. BEGLEITER: 8 Q. So you said "would have," but 9 you don't know? 10 A. If the statistical analysis, 11 and, again, subsequent -- looking at my reply 12 to the agency, there was no indication of an 13 inadvertent or advertent bias. 14 Q. This statistical analysis, do 15 you recall ever seeing this statistic analysis 16 prepared by Dr. Krah somewhere in this lab? 17 A. Not by Dr. Krah. It would have 18 come from the statistical group. In fact, 19 it's probably embedded in the full reply to 20 the agency and in subsequent discussions. 21 Q. We talked before about there 22 being at least two kinds of validation. I'm 23 not giving it to you yet. 24 A. He's not going to give it to me. 25 Q. Two kinds of validations, one</p>

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<p style="text-align: right;">Page 242</p> <p>1 for the assay and one for the lab itself? 2 A. Laboratory, yes. 3 Q. Are there any other kinds that 4 you're aware of? 5 A. Well, validation -- both the 6 terms validation and qualification are general 7 terms. So they relate to any set of 8 activities in which there is a requirement for 9 accuracy, precision and ability to interpret 10 the quantitative results, whether it be a 11 laboratory, whether it be an individual, 12 whether it be an assay. As an individual you 13 can be qualified and validated as well. 14 Q. Who did the validation for 15 Protocol 007, the PRN part of the test? 16 A. Well, the data for the 17 validation would have been generated by the 18 laboratory that developed the assay. 19 Q. Dr. Krah's laboratory? 20 A. That would have been Dr. Krah's 21 laboratory, yes. 22 Q. Okay. And did CBER request the 23 validation results for the neutralization 24 assays you were going to use? 25 A. I don't recall offhand, but I</p>	<p style="text-align: right;">Page 244</p> <p>1 analyzing the assays? 2 A. Yes, but that was my requirement. 3 That was the requirement, but it is not a 4 formal requirement -- so let me explain. It 5 is not a formal requirement that validation or 6 qualification be completed, be completed prior 7 to the actual conduct of the assay. It is a 8 requirement that it be completed prior to the 9 analysis of the data from the assay. So if 10 you develop an assay and you do not complete 11 the validation prior to actually running the 12 samples and you run the samples at risk 13 because you're doing the validation either 14 afterwards or in parallel, it's your risk. 15 Because once you run the samples, and if the 16 assay turns out not to be appropriately 17 validated following the validation protocol, 18 then you put the entire test and entire data 19 set at risk. 20 Q. Excuse me for one second. 21 In the case of 007, was the 22 validation experiments done by the same group, 23 same lab that was doing the assay, the PRN? 24 MS. DYKSTRA: Objection. 25 THE WITNESS: I cannot recall</p>
<p style="text-align: right;">Page 243</p> <p>1 would be very surprised if they had not 2 requested. It's a standard request from the 3 agency. 4 Q. Was the asset conducted before 5 or after assays were completed? 6 MS. DYKSTRA: Objection. 7 BY MR. BEGLEITER: 8 Q. Excuse me. Was the assay 9 conducted before or after the validation was 10 completed? 11 A. I don't recall offhand. 12 Q. Would that be something that 13 would be inappropriate, to complete the 14 validation before the -- 15 A. It's not. 16 Q. Let me finish the sentence. 17 A. I'm sorry. My apologies. 18 Q. -- before the validation was 19 completed? 20 A. I apologize. 21 It is not a requirement. 22 Q. Didn't you indicate before, we 23 were talking about Dr. Ward, that you would 24 have wanted his lab to be validated before he 25 was given the task of doing the clinical -- of</p>	<p style="text-align: right;">Page 245</p> <p>1 directly, but that would normally be 2 the case. 3 BY MR. BEGLEITER: 4 Q. It would normally be the case 5 that the same lab would do both, the 6 validation testing and the testing itself? 7 A. Yes. 8 Q. Can you go back to 20? The last 9 page, 8839. When you write, "It should be 10 noted that this assay was being performed by 11 the research personnel who developed the assay 12 and in the research laboratory..." 13 A. Yes. 14 Q. ...in which the assay was 15 developed. Typically, the assay should have 16 been transferred -- 17 A. Would have been transferred, not 18 should have been transferred. 19 Q. "...to a testing lab following 20 this development." 21 A. Yes. 22 Q. Isn't that referring to the 23 validation testing? 24 A. No, because recall, you have to 25 validate so you do it two different ways.</p>

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<p style="text-align: right;">Page 246</p> <p>1 Typically what you would do is that you would,</p> <p>2 if laboratory A, in this case, the research</p> <p>3 laboratory were to develop the assay, then</p> <p>4 they would perform a validation. Terminology</p> <p>5 used today is qualification. Means the same</p> <p>6 thing.</p> <p>7 So they would normally perform</p> <p>8 it to determine the assays, as we said,</p> <p>9 precision, accuracy, reproducibility. When an</p> <p>10 assay that is a validated assay is then</p> <p>11 transferred from one laboratory to another</p> <p>12 laboratory, the assay is revalidated to make</p> <p>13 sure that it behaves the way in which it</p> <p>14 behaved when it was first developed. So you</p> <p>15 would wind up basically revalidating the</p> <p>16 laboratories. So what normally would have</p> <p>17 been done in this case is the research</p> <p>18 laboratory would have developed the assay,</p> <p>19 would have qualified the assay, would have</p> <p>20 sent it to a testing laboratory, either</p> <p>21 internally or externally, and then the assay</p> <p>22 would have been requalified in the context of</p> <p>23 that testing laboratory probably at the same</p> <p>24 time that you would validate the laboratory</p> <p>25 itself.</p>	<p style="text-align: right;">Page 248</p> <p>1 both the lab running the assay and CBER would</p> <p>2 be the same.</p> <p>3 Q. Let me show you 682341 to</p> <p>4 682345.</p> <p>5 - - -</p> <p>6 (Exhibit Emini-22, List,</p> <p>7 00682341 - 00682345, was marked for</p> <p>8 identification.)</p> <p>9 - - -</p> <p>10 MS. DYKSTRA: Do you have</p> <p>11 copies?</p> <p>12 MS. MAHENDRANATHAN: Yes.</p> <p>13 BY MR. BEGLEITER:</p> <p>14 Q. The only question I'm going to</p> <p>15 have is what is this? Do you recognize this</p> <p>16 type of document?</p> <p>17 A. Yes. What this document is, is</p> <p>18 a document in which the operator of the assay</p> <p>19 will report their observations.</p> <p>20 Q. And this is part and parcel of</p> <p>21 actually doing the assay?</p> <p>22 A. This is part and parcel of</p> <p>23 performing the assay, yes.</p> <p>24 Q. Does it have a date on when this</p> <p>25 was performed?</p>
<p style="text-align: right;">Page 247</p> <p>1 Q. Wasn't -- didn't CBER want it --</p> <p>2 want to review and concur with the validation</p> <p>3 protocol before the testing?</p> <p>4 MS. DYKSTRA: Objection.</p> <p>5 THE WITNESS: Again, it is --</p> <p>6 the reason why I'm hesitating in</p> <p>7 answering your question is that that is</p> <p>8 not a formal requirement. CBER may ask</p> <p>9 to view a validation protocol, a</p> <p>10 validation data prior to the actual</p> <p>11 running of an assay. However, and this</p> <p>12 has happened to me on multiple</p> <p>13 occasions, CBER will also say go right</p> <p>14 ahead, if you want to run the assay</p> <p>15 prior to the time that we looked at the</p> <p>16 validation, but you run it at your own</p> <p>17 risk.</p> <p>18 BY MR. BEGLEITER:</p> <p>19 Q. Does CBER usually approve or</p> <p>20 concur with the validation?</p> <p>21 A. CBER would have to approve --</p> <p>22 would have to concur that the validation was</p> <p>23 done correctly and that the numbers that were</p> <p>24 being reported from the assay, that the way in</p> <p>25 which one would interpret those numbers by</p>	<p style="text-align: right;">Page 249</p> <p>1 A. 9th of February, 2001.</p> <p>2 Q. And do you know when the</p> <p>3 validation protocol was given to --</p> <p>4 A. I don't recall.</p> <p>5 Q. Let me finish the question.</p> <p>6 When the validation protocol was</p> <p>7 given to CBER?</p> <p>8 A. I apologize.</p> <p>9 I do not recall.</p> <p>10 Q. I should point out on that</p> <p>11 document, 2341, at the bottom it says, "Mary</p> <p>12 Yagodich, December 12, 2000," at the bottom.</p> <p>13 Do you see that?</p> <p>14 A. It says, "December 12, 2000," at</p> <p>15 the bottom.</p> <p>16 Q. Right. Let me show you again</p> <p>17 Exhibit 6. You have that in front of you?</p> <p>18 A. 6?</p> <p>19 Q. Yeah.</p> <p>20 A. Yes.</p> <p>21 Q. And go to page 17080.</p> <p>22 A. Yes.</p> <p>23 Q. And that shows -- what is this</p> <p>24 document, that 17080?</p> <p>25 A. This is a document to Dr. Krah</p>

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<p style="text-align: right;">Page 250</p> <p>1 from the statistical analysis group that is -- 2 refers to the validation of the plaque 3 reduction neutralization assay. And it refers 4 to the validation results. Just bear with me 5 a second, let me go look. Yes, this refers to 6 the validation results, yes. 7 Q. Of the PRN? 8 A. Of the PRN, plaque reduction 9 neutralization. 10 Q. If you go to the second page of 11 the exhibit, there's a letter. 12 A. Of the overall exhibit, yes. 13 Q. Yes, the whole entire exhibit. 14 And that letter is dated March 12, 2001? 15 A. That is dated March 12, 2001. 16 Q. So it's some two months plus 17 after Exhibit 23 was prepared. Is that right? 18 A. Exhibit 22. 19 Q. Exhibit 22 was prepared. 20 A. Yes. 21 Q. And it's your statement that 22 that was perfectly okay? 23 A. Yes. 24 Q. But at the risk of Merck? 25 A. But it is at the risk of -- it</p>	<p style="text-align: right;">Page 252</p> <p>1 which the FDA, CBER were told that assays were 2 completed before the -- excuse me, the assays 3 were conducted -- 4 A. The assays -- 5 Q. Let me start again. 6 Do you recall from anyplace, 7 whether it's a document, a conversation in 8 memory, that CBER was told that assays were 9 conducted prior to CBER receiving the 10 validation protocol for concurrence? 11 A. I do not recall a direct 12 communication with CBER noting exactly what 13 you said, but it's self evident. 14 Q. Do you recall CBER being told 15 when the individual assays were conducted? 16 MS. DYKSTRA: Objection. 17 THE WITNESS: I do not recall, 18 but it's in the workbook, the dates. 19 BY MR. BEGLEITER: 20 Q. The workbook, you're referring 21 to Exhibit 23? 22 A. Exhibit 22. 23 Q. 22. Was the workbook given to 24 the FDA? 25 MS. DYKSTRA: Objection.</p>
<p style="text-align: right;">Page 251</p> <p>1 is at the risk of the company. As, again, 2 validation is required and accepted by the 3 agency prior to the time that the data that 4 you see here in Exhibit Number 22 can be 5 analyzed by the statistician in the end. But 6 the actual generation of the data, that occurs 7 at your risk. So if you're not willing to 8 take the risk, you wait until the validation 9 is completed and accepted by the agency. If 10 you believe that your assay is validate-able 11 or qualifiable, means the same thing, then if 12 you are pressed for time, you can take the 13 risk of running it. The risk, of course, 14 being that the validation may not work out or 15 the agency may not except the validation. 16 Q. So my question to you is, were 17 you informed that Dr. Kraus was taking this 18 risk for Merck? 19 MS. DYKSTRA: Objection. 20 THE WITNESS: I do not recollect 21 being informed either that he was or 22 that he was not. I don't recall. 23 BY MR. BEGLEITER: 24 Q. Do you recall anyplace in which 25 any conversation, any document, anyplace in</p>	<p style="text-align: right;">Page 253</p> <p>1 THE WITNESS: I don't recall if 2 the workbook was given to the FDA, but 3 I do know that this was part of the 4 data, I presume, I don't know if it was 5 exactly this data, but part of the data 6 that the FDA inspector came to observe 7 and upon which she noted the concern 8 over the apparent changes without 9 written justification. 10 BY MR. BEGLEITER: 11 Q. That wasn't my question. My 12 question was whether the FDA would -- CBER was 13 told? 14 A. As I said -- I'm sorry. 15 MS. DYKSTRA: I said let him 16 finish. 17 BY MR. BEGLEITER: 18 Q. That CBER was told that assays 19 were completed prior to the -- to sending 20 the -- to Merck sending the validation 21 protocol to CBER? 22 MS. DYKSTRA: Objection. Asked 23 and answered. 24 BY MR. BEGLEITER: 25 Q. Well --</p>

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<p style="text-align: right;">Page 254</p> <p>1 A. I do not have a direct 2 recollection of such a communication. 3 Q. I believe I asked you this 4 morning whether you signed any of the 5 validation protocols for PRN 007. Let's take 6 a look at 33 -- 337307. 7 I'm asking the reporter to mark 8 for identification 337307 through 337313. 9 - - - 10 (Exhibit Emini-23, Plaque 11 Reduction Neutralization Assay for 12 Mumps, 00337307 - 00337318, was marked 13 for identification.) 14 - - - 15 BY MR. BEGLEITER: 16 Q. So what is this document? 17 A. This is -- allow me a moment, 18 please. These are signature pages on the 19 front end of the document related to Plaque 20 Reduction Neutralization Assay, Analytical 21 Validation Protocol Version 2. I don't know 22 exactly which plaque reduction neutralization 23 assay was being referred to here. This is the 24 AIGENT assay according to this document which 25 is the anti-IgG neutralization assay.</p>	<p style="text-align: right;">Page 256</p> <p>1 Q. What page are you looking at, 2 the number at the bottom? 3 A. My apologies. I'm looking at 4 page 17080. 5 Q. Going back -- so when you signed 6 it, when you signed this document -- 7 withdrawn. 8 What does your signature on this 9 document mean? 10 MS. DYKSTRA: Exhibit 33. 23. 11 THE WITNESS: 23, that is 12 correct. It means that I am in 13 concurrence with the plan to conduct 14 the validation as indicated in the 15 documents, number 23. 16 BY MR. BEGLEITER: 17 Q. The plan to conduct the validation? 18 A. The plan to -- yes. This is the 19 validation protocol. So Number 23 is the 20 protocol that describes how the validation 21 will be conducted. 22 Q. That's why if you turn to page 23 315 -- 24 A. 15? 25 Q. Yeah. Let's say purpose. Let</p>
<p style="text-align: right;">Page 255</p> <p>1 Q. This is the assay that we have 2 been discussing, yes, the PRN? 3 A. Yes. 4 Q. And do you see your signature on 5 it? Well, do you see your signature on any of 6 these sheets? 7 A. Yes, I do. 8 Q. And you signed it what day? 9 A. The 22nd of February 2001. 10 Q. And you had no comments? 11 A. I had -- specifically says none. 12 Q. So, sir, you'll notice we talked 13 about the validation protocols being sent to 14 the -- being sent to CBER in March of 2000 -- 15 March of 2001? Going back to that document. 16 A. I need to go back, please. 17 MS. DYKSTRA: Exhibit 6. 18 BY MR. BEGLEITER: 19 Q. Exhibit 6, the cover letter 20 March 12th. 21 A. The cover letter was March 12, 22 2001, yes. And the results of the validation 23 were completed on February -- the memo from 24 the statistical group that was being 25 referenced is dated February 27, 2001.</p>	<p style="text-align: right;">Page 257</p> <p>1 me read to you the sentence in the -- the 2 second sentence. The data rising from this 3 validation study will be used to 1, 2, 3, 4, 4 5, do you see that? 5 A. Yes. 6 Q. So that means it hadn't been 7 done yet? 8 A. That is correct. This is the 9 protocol for conducting -- 10 Q. On page -- the next page, 316, 11 at the bottom "Assay Validation Experiments," 12 the second sentence -- the first sentence, 13 "The plaque reduction neutralization assay 14 will be performed..." And then the next 15 sentence, "The validation experiment will 16 include..." So this is all speaking in 17 future tense? 18 A. Yes, of course. 19 Q. Do you know when it was 20 completed? 21 MS. DYKSTRA: Objection. Form. 22 THE WITNESS: Well, the -- 23 sorry. 24 MS. DYKSTRA: Objection. Form. 25 THE WITNESS: I'm sorry. Well,</p>

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<p style="text-align: right;">Page 258</p> <p>1 my only answer to that comes from 2 looking at the document in your Exhibit 3 Number 6 which was a response to the 4 agency and going to page 80 which was 5 the data that was the completion of the 6 validation assay dated approximately -- 7 dated exactly seven days later, on 8 February 27, 2001. 9 BY MR. BEGLEITER: 10 Q. On the document that you signed, 11 is that a template or is that something that 12 was drafted just for this assay? 13 MS. DYKSTRA: Objection. Form. 14 THE WITNESS: I -- well, clear 15 what's your question, sir, you were 16 referring to what? Are you referring 17 to -- 18 BY MR. BEGLEITER: 19 Q. The signature page. 20 A. You're referring to the 21 signature page? 22 Q. Yes. 23 A. So we reference the signature 24 page, well, it is specific for this assay 25 insofar as the names on the signature page are</p>	<p style="text-align: right;">Page 260</p> <p>1 only thing that the signature page indicates 2 is that there is approval, as long as no 3 comments are made by the individuals who sign. 4 That the validation protocol as written is 5 acceptable and can, in fact, be used to 6 validate the assay as described. Again, there 7 is also a risk factor associated with this 8 because if it is approval after the validation 9 is actually -- if an issue is raised by any of 10 the individuals that were being asked to 11 review. If an issue was raised after the 12 actual validation protocol is run, then one 13 has to go back and one has to do it all over 14 again. 15 Q. The document Number 23 has a box 16 on the top, it says, "Initial Review," it's 17 bolded and there's a box. 18 A. Yes, I see it. 19 Q. And then to the right of that 20 there's "Final Review" in grayish letters. 21 A. Yes. 22 Q. What is the initial review? 23 A. I don't recollect offhand what 24 the difference between the initial review and 25 final view. This is a four-page document, so</p>
<p style="text-align: right;">Page 259</p> <p>1 present. 2 Q. Going back -- 3 A. Because they were specific 4 obviously to the laboratory and the reporting 5 relationships. 6 Q. Going to 23 it says Jerry Sadoff 7 N/A. Do you know what that mean? 8 A. Jerry Sadoff was -- had 9 responded. He was in the clinical research 10 group. N/A means he was not available. 11 Q. If he was listed on this 12 document for a signature, shouldn't his 13 name -- shouldn't he have -- he eventually 14 signed off? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: Not necessarily 17 so. It all depends upon what the 18 company was using as an acceptable 19 representation of review and signature. 20 BY MR. BEGLEITER: 21 Q. Even though there was at least 22 seven days between the time you signed it and 23 the time that the experiments were completed? 24 A. Right, but it's also acceptable 25 to sign post facto, too, as long as -- the</p>	<p style="text-align: right;">Page 261</p> <p>1 the initial review and final review would most 2 likely be exactly the same. 3 Q. You're speculating now? 4 A. I am totally speculating. It's 5 a four-page document, pretty straightforward 6 to review. 7 Q. Do you know if you ever signed 8 off on a, quote/unquote, final review? 9 A. I don't have any recollection. 10 Q. If you take a look at page 7314, 11 the very bottom there's Karen Hencken's 12 signature. I believe above the word "Comments" 13 there's something that looks like a check 14 mark? 15 A. Yes. 16 Q. Do you know if she had any 17 comments? 18 A. I don't know. I can only go by 19 what she has here which was there was nothing 20 there. 21 Q. This was a validation protocol 22 for a clinical trial using clinical samples 23 for children. Is that correct? 24 A. This was a validation protocol 25 for an assay that would be used to generate</p>

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<p style="text-align: right;">Page 262</p> <p>1 data from a clinical study. 2 Q. Did you understand that the 3 validation protocol authorized the experiments 4 to be conducted in a GLP compliant lab? 5 MS. DYKSTRA: Objection. 6 THE WITNESS: All validation 7 studies and all clinical assay studies 8 are to be conducted in laboratories 9 that follow good -- GLP refers to good 10 laboratory practice, it means a 11 different thing today than it did then, 12 but... 13 BY MR. BEGLEITER: 14 Q. Yes. And, in fact, was Dr. Krah's 15 lab a GLP compliant lab? 16 A. The laboratory -- the GLP 17 compliance required the presence of SOPs and 18 the requirement to follow SOPs, so my answer 19 to that question would be yes. 20 Q. Is there a certification for 21 GLP? 22 A. There is no formal certification 23 as far as I'm aware for GLP. 24 Q. And a clinical trial involving 25 clinical samples in children must be conducted</p>	<p style="text-align: right;">Page 264</p> <p>1 yes. 2 Q. And did you ever sign any 3 validation of Dr. Krah's lab and personnel to 4 run a -- to run the clinical samples pursuant 5 to GCP? 6 A. Again, GCP does not refer to the 7 laboratory or to the laboratory operations. 8 What is being used in some of these documents 9 in a very loose fashion is the term GLP which 10 refers to good laboratory practices. In 11 general what this refers, and this is typical 12 of all laboratories that run clinical assays, 13 is that they run a validated assay and that 14 the laboratory's operations are run under 15 specified standard operating procedures. 16 Q. Do you know if the personnel in 17 Dr. Krah's lab had been trained to perform 18 assays under GMP or GCP? 19 A. If the individuals followed the 20 standard operating procedures and ran the 21 validated assay in the way in which the assay 22 was defined by the SOP in a validated fashion, 23 that would have been acceptable. 24 Q. But you don't know if, in fact, 25 that occurred?</p>
<p style="text-align: right;">Page 263</p> <p>1 according to a -- to good clinical practices. 2 Isn't that correct? 3 MS. DYKSTRA: Objection. 4 THE WITNESS: The conduct of the 5 clinical trial has to be by good 6 clinical practices, yes, which are 7 again, you know, clear specifications 8 in terms of what that means. 9 BY MR. BEGLEITER: 10 Q. Do you know if Dr. Krah's lab 11 was a good clinical practices laboratory? 12 A. Dr. Krah was -- good clinical 13 practices refers to the conduct of the 14 clinical trial, the interaction with the 15 subjects of the trial, what one does with 16 those interactions, issues of institutional 17 review board approvals, issues of ethics. It 18 does not relate to the laboratory. It does 19 not relate to the laboratory. It relates to 20 the conduct with the subjects in the study. 21 Q. Let me see if we can get this 22 straight. The same lab with the same 23 personnel and SOP were used to develop, 24 validated and perform the assays. Right? 25 A. In the case of the 007 study,</p>	<p style="text-align: right;">Page 265</p> <p>1 A. If there was what, formal 2 training? 3 Q. Yes. 4 A. I do not recollect if there was 5 formal training involved, but it is not a 6 requirement. 7 Q. Well, I thought you said that it 8 was a requirement for a GLP? 9 A. That standard operating 10 procedures be followed. Now, whether or not 11 one actually has a formal training for that or 12 not is another story. 13 MS. DYKSTRA: Let me know when 14 it's a good time to take a break. 15 MR. BEGLEITER: I'm almost 16 finished with this subject. 17 I'll hand the court reporter 18 Merck 780051 through 54. 19 - - - 20 (Exhibit Emini-24, E-mail 21 exchange, 00780051 - 00780054, was 22 marked for identification.) 23 - - - 24 BY MR. BEGLEITER: 25 Q. You didn't receive this document,</p>

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1 did you?
 2 A. I did not, no.
 3 Q. I'm asking, do you know who
 4 Robin Mogg is?
 5 A. I do not recall directly. I
 6 recognize the name, but I do not recall the
 7 individual.
 8 Q. How about Joseph Antonello?
 9 A. Joseph Antonello was a member of
 10 the statistical group.
 11 Q. This document purports to give
 12 the dates of the asset runs, isn't that
 13 correct, regarding -- purports to give the
 14 dates of the asset runs?
 15 A. Of the assay runs.
 16 Q. Assay, I'm sorry.
 17 A. Asset refers to something else.
 18 MS. DYKSTRA: I'm sorry, Bob, is
 19 there a question pending?
 20 MR. BEGLEITER: I'm sorry, I
 21 thought he was still looking at it. I
 22 think he is still looking at it.
 23 MS. DYKSTRA: I'm sorry, your
 24 question was?
 25 MR. BEGLEITER: I'm showing him

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1 the document. Before I ask any
 2 question, I'm going to give him a
 3 chance to look at it, the document.
 4 MS. DYKSTRA: Okay. I was
 5 asking whether there was a question
 6 pending. I wasn't sure.
 7 MR. BEGLEITER: There's no
 8 question pending.
 9 THE WITNESS: Okay. Thank you.
 10 BY MR. BEGLEITER:
 11 Q. And does this show in Protocol
 12 007 the dates, at least, of some of the assay
 13 runs?
 14 A. This shows the dates, if I read
 15 this correctly, it's pretty sparse, relates to
 16 the assay runs that were performed in the
 17 context of the assay validation.
 18 Q. And the earliest for the
 19 pediatrics were August 21, 2000. Is that
 20 right?
 21 A. According to this, it would be
 22 for what it says here, August 21, 2000. But I
 23 don't know what that entry refers to.
 24 Q. Can you explain to me -- do you
 25 have any explanation as to why the validation

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1 wasn't completed and sent to CBER until
 2 March 12, 2001?
 3 MS. DYKSTRA: Objection.
 4 THE WITNESS: Why it was not
 5 sent?
 6 BY MR. BEGLEITER:
 7 Q. Yes.
 8 A. I can't tell you why it was not
 9 sent other than to say there was no requirement
 10 to send it.
 11 Q. Well, it's about a seven-month
 12 period from the first pediatric run until it
 13 goes to --
 14 A. I don't know what this pediatric
 15 run refers to. I really don't. The only
 16 thing that I can ascertain from this were the
 17 validation runs that were run from -- the
 18 so-called adult runs at the top that were run
 19 from the 18th of January to the 26th of
 20 February 2001. So that would have -- those
 21 would have been runs that were run -- studies
 22 that were run, you know, roughly at -- but
 23 these are adult runs. So this refers to assay
 24 runs. Whether or not they're directly related
 25 to the validation or not, I cannot tell from

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1 this.
 2 Q. There's no question, though,
 3 that the validation could have been done prior
 4 to when it was done?
 5 MS. DYKSTRA: Objection. Form.
 6 THE WITNESS: Well, anything can
 7 be done at any time.
 8 BY MR. BEGLEITER:
 9 Q. That's true. What about -- I
 10 mean, the fact that we -- I showed you an
 11 assay that was run in December. I'm trying to
 12 understand why maybe you -- you tell me that
 13 it wasn't necessary --
 14 A. It was not necessary.
 15 Q. -- but I want to understand why
 16 it was that assays were done and then the
 17 validation went in?
 18 A. Well, when -- so I will give you
 19 a hypothetical circumstance under which one
 20 would normally do that. Hypothetical
 21 circumstances could be one in which an assay
 22 is developed. One is confident about the
 23 parameters of the assay. There is a time
 24 pressure of some sort to generate the data
 25 from the assay. Following the procedure of

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<p style="text-align: right;">Page 270</p> <p>1 performing a formal validation and then 2 sending the data and then obtain concurrence 3 to the agency prior to actually doing the run 4 takes time. Now, from a risk perspective, 5 that's the least risky approach, because if 6 there is a disagreement with the agency, then 7 one has the opportunity to go back and modify 8 the assay, redo the validation, whatever the 9 case happens to be. But once the assay 10 samples are run, the actual study samples are 11 run, you can't go back and do it over again. 12 So, therefore, you take a risk. 13 So if there's a time constraint 14 and I need to update it by a certain time, 15 what one would do is to validate the assay in 16 parallel, more or less in parallel with 17 running the actual clinical samples, it could 18 be more or less, because it would be a little 19 bit before, it could be a little bit after. 20 The only point is you would not complete the 21 validation prior to actually generating data 22 on the actual clinical samples. 23 Q. Do you recall if there was a 24 time constraint with 007? 25 A. Well, there were time constraints</p>	<p style="text-align: right;">Page 272</p> <p>1 constraint? 2 A. Specifically why there was any 3 kind of time constraint, in specific 4 discussions that I had recollect today, the 5 answer is no. 6 Q. Now, you mentioned that there 7 were -- I promised you we could break, so 8 let's break. 9 VIDEOGRAPHER: The time is now 10 4:02. We're going off the video 11 record. 12 - - - 13 (A recess was taken.) 14 - - - 15 VIDEOGRAPHER: The time is 4:17. 16 We're back on the video record. 17 BY MR. BEGLEITER: 18 Q. Doctor, was it generally 19 understood at Merck -- withdrawn. 20 Your view that Merck could do 21 the assay, test the assays and then do the 22 validation, was that written somewhere? Is 23 there any kind of rule for that that we can 24 look at? 25 A. Is there any written rule that</p>
<p style="text-align: right;">Page 271</p> <p>1 related, but I don't know if they were related 2 to this. There were time constraints 3 associated with generating data from that 4 so-called interim analysis to have a look at 5 the seroconversions that were present that -- 6 that the seroconversions that were elicited in 7 subjects who received vaccine of certainly the 8 two lower potency values that were being 9 assessed in the study. 10 Q. Because children had received 11 vaccines below the 4.3 spec, is that what 12 you're saying? 13 MS. DYKSTRA: Objection. Form. 14 THE WITNESS: Because there was 15 a -- again, I do not recollect exactly, 16 but whatever it was there was a desire 17 to generate data. I really don't 18 recollect the discussions, but there 19 was a desire clearly to generate data 20 to assess the seroconversion as 21 measured by the assay in those two 22 lower potency values. 23 BY MR. BEGLEITER: 24 Q. You don't know sitting here 25 today why there was any kind of time</p>	<p style="text-align: right;">Page 273</p> <p>1 I'm aware of? No. 2 Q. So where do you get the idea 3 that it's appropriate for -- it's permissible? 4 A. It's permissible. I mean, it's 5 standard, it's standard practice. I've had 6 other examples, not necessarily when I was at 7 Merck, but in my subsequent employment, I'll 8 leave it at that, where we've done the same 9 thing, run assays at risk before there is 10 agreement with the agency on the validation. 11 Q. Shouldn't you have approved this 12 at risk running? 13 MS. DYKSTRA: Objection. 14 THE WITNESS: Not necessarily 15 formally approved it. I may have 16 approved it informally. I just simply 17 do not recollect. 18 - - - 19 (Exhibit Emini-25, 1/4/02 E-mail 20 with attachment, 00579518 - 00579521, 21 was marked for identification.) 22 - - - 23 BY MR. BEGLEITER: 24 Q. I'm going to show you a document 25 that's been marked Emini-25. It's Merck</p>

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1 579518 through 521. You'll find it an easy
 2 read. It's been mostly redacted.
 3 A. Okay.
 4 Q. First of all, did you receive
 5 this document in the usual course of your
 6 employment with Merck?
 7 A. If it was sent to me, I'm
 8 looking for that right now.
 9 Q. Look at five lines from the top.
 10 A. There's many names there. Yes,
 11 there I am. So, therefore, the answer to your
 12 question is yes.
 13 Q. And it says, "Attached are the
 14 minutes of the December 12 meeting of the
 15 Critical Assay Subcommittee. Thanks Joan."
 16 [As read] Who is Joan Staub?
 17 A. Joan Staub was -- she had
 18 multiple positions within the organization.
 19 So -- and she was in the, if I remember
 20 correctly, in the project management group, or
 21 the program management group, whatever it was
 22 called.
 23 Q. Now, behind that is an e-mail
 24 dated January 4, 2001. I won't ask you any
 25 questions regarding this.

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1 A. Please don't.
 2 Q. Turn to the second page.
 3 "Update: CBER Audit of Mumps Neutralization
 4 Data."
 5 Do you see that?
 6 A. Right.
 7 Q. Now, I'm going to read to you
 8 the first sentence. As a result of the data
 9 audit, CBER believes that we used technical --
 10 clinical trial sera to develop the assay and
 11 that we changed the assay after we looked at
 12 the data. Do you see that?
 13 A. Yes.
 14 Q. This is a very -- would you
 15 agree this is a pretty strong accusation?
 16 MS. DYKSTRA: Objection.
 17 THE WITNESS: No, it's not an
 18 accusation. It says that CBER believes
 19 that we used clinical trial sera.
 20 Remember, it depends on the context in
 21 which the individual wrote the
 22 statement. The way I would interpret
 23 this is to say that CBER has a concern
 24 that the assay could have been changed
 25 after we looked at the data Joan

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1 derived from the clinical trial sera.
 2 BY MR. BEGLEITER:
 3 Q. If that were, in fact, done,
 4 that would be a pretty serious scientific
 5 violation?
 6 MS. DYKSTRA: Objection.
 7 THE WITNESS: That would be
 8 probably something you consider to be
 9 inappropriate, yes.
 10 BY MR. BEGLEITER:
 11 Q. More than inappropriate. That
 12 would be a violation of the ethics of
 13 scientists?
 14 MS. DYKSTRA: Objection.
 15 THE WITNESS: Well, ethics is a
 16 strong term. I would call it, I would
 17 call it inappropriate and not something
 18 that one would normally do or should
 19 normally do.
 20 BY MR. BEGLEITER:
 21 Q. And did that happen?
 22 A. Not to my recollection. In
 23 fact, that did not happen.
 24 Q. You believe it didn't happen?
 25 A. I believe that it didn't happen

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1 for the reasons noted here.
 2 Q. "We can document, using D.
 3 Krah's...," that's Dr. Krah, right,
 4 "...notebook, that we developed the assay with
 5 laboratory sera and we can build an argument
 6 that the assay was validated before we started
 7 running."
 8 A. That was Joan Staub's opinion on
 9 the matter.
 10 Q. Well, the opinion here is that
 11 it was -- withdrawn.
 12 This indicates that it would be
 13 a useful thing to build an argument that the
 14 assay was validated before the assay started
 15 running. Isn't that right?
 16 MS. DYKSTRA: Objection.
 17 THE WITNESS: That was Joan
 18 Staub's opinion because this is a note
 19 written by her.
 20 BY MR. BEGLEITER:
 21 Q. So she has an opinion and you
 22 have an opinion?
 23 A. And other people may have had
 24 other opinions.
 25 Q. Right. Okay.

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<p style="text-align: right;">Page 278</p> <p>1 A. So this would certainly not be 2 my perspective. 3 Q. Now, do you know what a summary 4 report is of a validation protocol? 5 A. Exactly what it says. It is a 6 report of the validation study that was done. 7 Q. Was one done for Protocol 007? 8 A. I don't recall if -- well, there 9 was a report -- there was a report that we 10 noted in my reply to the CBER 483 from the 11 statistical group, I believe that's what 12 you're referring to. 13 Q. Did you write that summary 14 report or did somebody else? 15 A. No. That would have been 16 written by the statistical group. 17 Q. Is that Mr. Antonello's group? 18 A. That would have been 19 Mr. Antonello's group. 20 Q. Going back to 23, a document 21 that you signed at least on the second page of 22 it, I just want to make sure I understand 23 this. The third sentence at the top, "It is 24 understood that these experiments will be 25 performed in a GLP compliant laboratory to</p>	<p style="text-align: right;">Page 280</p> <p>1 MS. DYKSTRA: Objection. 2 THE WITNESS: Okay. Yes. 3 BY MR. BEGLEITER: 4 Q. You know about that? 5 A. Well, it would be a standard 6 operation to be conducted but that refers to 7 the clinical investigator. The way he 8 described it specifically to the clinical 9 investigator and the testing referred to there 10 would be testing performed by the clinical 11 investigator. 12 MR. BEGLEITER: Let's get this 13 one. 126340. Let's have it marked. 14 It's 24. I'm asking the court reporter 15 to mark as an exhibit Merck 126340 16 through Merck 126351. 17 - - - 18 (Exhibit Emini-26, 2/5/02 Letter 19 with attachments, 00126340 - 00126351, 20 was marked for identification.) 21 - - - 22 BY MR. BEGLEITER: 23 Q. Your name is not in this 24 document. Are you familiar with the forms 25 that are attached here?</p>
<p style="text-align: right;">Page 279</p> <p>1 ensure the validity of the data." Okay. And 2 was it your testimony that in order to be a 3 GLP compliant laboratory you needed an SOP? 4 A. You needed to operate in the 5 context of existing, approved and filed 6 standard operating procedures, yes. And they 7 could relate to any one of a number of 8 different factors in the laboratory. 9 Q. Okay. Isn't GLP reserved for 10 testing in the experimental non-clinical 11 research arena? 12 A. The way the terminology is used 13 today, yes. It is used specifically to refer 14 to that. Back in the day, 20 years ago, the 15 terminology was used much more loosely. 16 Q. Do you know what Form 1572 is? 17 A. I don't recall off the top of my 18 head, no. 19 Q. Is there a form that a principal 20 investigator and the study sponsor are 21 required to sign committing to conduct the 22 study under accepted norms including GCP 23 compliance, not just with regard to the 24 subjects but with all testing? Does that ring 25 a bell?</p>	<p style="text-align: right;">Page 281</p> <p>1 A. Allow me a moment. 2 Q. Investigational New Drug 3 Application. 4 A. That is your standard IND form 5 that goes with all correspondence associated 6 with an open IND, as was the case here. And 7 then there's a form related to the statement 8 of investigator. In this case it was a 9 protocol amendment related -- I'm just reading 10 what's in the memo. And the note related to a 11 new clinical investigator, new clinical side 12 being brought on board, into the study. 13 Q. To your knowledge, was a 1572 14 form filled out for MMR II Protocol 007? 15 MS. DYKSTRA: Objection. 16 BY MR. BEGLEITER: 17 Q. If you know. 18 A. I don't know -- so this is a 19 Form FDA 1572 but relating specifically to 20 this single investigator, April Palmer, MD. 21 Q. Notice on the front page it does 22 make reference to Protocol 007. It gives the 23 title of it. 24 A. Yes, that's right. And 25 presumably this form would have been filled</p>

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<p style="text-align: right;">Page 282</p> <p>1 out by all the other investigators involved in 2 the study as well. 3 Q. And does this form contain a 4 commitment that the study sponsors required -- 5 is committed to conduct the study under 6 accepted norms including good clinical 7 practice compliance? 8 A. Would you, please, point that 9 out to me? 10 Q. Under "COMMITMENTS"? 11 A. Yes. 12 Q. "I agree to conduct the 13 study(ies) in accordance with the relevant, 14 current protocol(s) and will only make changes 15 in a protocol after notifying the sponsor, 16 except when necessary to protect the safety, 17 rights, or welfare of subjects." 18 Do you see that? 19 A. Yes, I do. 20 Q. Are you familiar with 21 CFR 21 part 50? 22 A. I am not specifically familiar 23 with the details of that particular part of 24 the CFR. 25 Q. Move on.</p>	<p style="text-align: right;">Page 284</p> <p>1 Q. Was this a regular occurrence 2 where you would bring in entire labs, people 3 and have discussions with them? 4 MS. DYKSTRA: Objection. 5 THE WITNESS: It would not be an 6 unusual occurrence. 7 BY MR. BEGLEITER: 8 Q. And was the lab in a different 9 building from your office? 10 A. I recollect that the laboratory 11 was in the same building as my office. It 12 would have been building 16. 13 Q. Did there come a time when you 14 met with them, with Dr. Krah's -- excuse me, 15 with the lab personnel in Dr. Krah's 16 laboratory and advised them to follow 17 Dr. Krah's orders? 18 MS. DYKSTRA: Objection. 19 THE WITNESS: As I mentioned, I 20 have no recollection of direct -- of 21 any such meeting -- of any meeting, 22 period. 23 BY MR. BEGLEITER: 24 Q. Do you have any recollection of 25 discussing bonuses with any members of</p>
<p style="text-align: right;">Page 283</p> <p>1 A. Again, these are commitments 2 that relate specifically by Dr. Palmer to 3 Dr. Palmer. 4 Q. You mentioned a couple of times 5 you had a conversation with Steve Krahling 6 before the unannounced inspection? 7 A. Again, not direct recollection 8 of the conversations themselves, per se, but 9 upon review of documents. 10 Q. Now, we discussed before, I 11 don't know whether you agree or not, that 12 there were some problems in the lab with 13 personnel and the way the lab was being run. 14 MS. DYKSTRA: Objection. 15 BY MR. BEGLEITER: 16 Q. Actually in e-mails where there 17 was some criticisms? 18 A. Yes, there was, that's right. 19 You showed me e-mails where there was some 20 criticism. 21 Q. And did there come a time when 22 you invited Dr. Krah's lab to come to your 23 office to meet with them? 24 A. Again, I have no recollection of 25 the event.</p>	<p style="text-align: right;">Page 285</p> <p>1 Dr. Krah's lab? 2 MS. DYKSTRA: Objection. Asked 3 and answered. 4 THE WITNESS: I have no 5 recollection. 6 BY MR. BEGLEITER: 7 Q. Do you have any recollection of 8 discussing double bonuses with people in 9 Dr. Krah's lab? 10 A. That's the same question. I 11 have no recollection. 12 Q. Now, you saw documents where 13 Dr. Shaw advised you that people in Dr. Krah's 14 lab were working very hard -- 15 A. Yes. 16 Q. -- including nights, weekends 17 and holidays? 18 A. Yes. 19 Q. Did you ever tell anybody, 20 whether it's the entire lab or just 21 individuals, that there was a fall of 2001 22 deadline to get Protocol 007 completed? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: I have no 25 recollection.</p>

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<p style="text-align: right;">Page 286</p> <p>1 BY MR. BEGLEITER: 2 Q. Whether you told them or not, 3 was there any kind of deadline, whether 4 imposed by CBER or self imposed by Merck? 5 A. Well, again, based upon review 6 of the documents and overall what was 7 happening at the time, did it, in fact, appear 8 to be a deadline, yes. 9 Q. My question was, was it a 10 self-imposed deadline or was something that 11 CBER wanted? 12 A. That I cannot answer because 13 that I really don't know the answer to. I 14 don't know if it came out as a result of a 15 discussion with CBER or if the company decided 16 that it needed to be self imposed for some 17 reason. 18 Q. What kind of stresses did that 19 cause to get this thing, to get it done by a 20 certain date? 21 MS. DYKSTRA: Objection. 22 THE WITNESS: You have to be 23 more specific than that. Stress is -- 24 BY MR. BEGLEITER: 25 Q. Do you recall what the deadline</p>	<p style="text-align: right;">Page 288</p> <p>1 MS. DYKSTRA: Objection. Asked 2 and answered. Go ahead, you can 3 answer. 4 THE WITNESS: Thank you. Upon, 5 again, review of documents, I was shown 6 a memo that Mr. Krahling had written to 7 me concerning HR and personnel-related 8 issues in the laboratory, or 9 observations that he had that concerned 10 him. 11 BY MR. BEGLEITER: 12 Q. Who did you get the memo from? 13 A. If I remember correctly, it was 14 directly from Mr. Krahling. 15 Q. Who brought you the memo? 16 A. Oh, I can't -- I don't recall. 17 It may have been sent by e-mail. It could 18 have been an e-mail actually. I don't even 19 remember. 20 Q. You mentioned Bob Suter. Did 21 you discuss Mr. Krahling with Bob Suter at any 22 point? 23 MS. DYKSTRA: Objection. 24 THE WITNESS: I may have. 25 Again, I cannot recollect the specific</p>
<p style="text-align: right;">Page 287</p> <p>1 was to get Protocol 007 completed? 2 A. Would I surmise it that the 3 deadline -- no, I don't know what the exact 4 deadline was, but that there was certainly a 5 date in order to be able to get results by a 6 given day. 7 Q. And you don't -- 8 A. I can't give you a specific date 9 because I don't remember. 10 Q. Can you give the reason why that 11 was done at all? 12 A. As I said, other than the -- it 13 was there, I don't recall the reason for it. 14 Q. When did you first meet Steve 15 Krahling? 16 A. I gather, to the best of my 17 current recollection, it would have been right 18 after he joined the laboratory. 19 Q. Did you visit the laboratory? 20 A. I recall being in the laboratory 21 on a couple of visits, but I cannot recall the 22 context. 23 Q. Did there come a time when 24 Mr. Krahling contacted you for any purpose? 25 A. Again, upon --</p>	<p style="text-align: right;">Page 289</p> <p>1 event where I sat down with Mr. Suter 2 to discuss Mr. Krahling. 3 BY MR. BEGLEITER: 4 Q. Did you discuss Joan Wlochowski 5 with Mr. Suter? 6 A. I have no recollection of the 7 specific event. 8 Q. How long had you worked -- 9 withdrawn. 10 Was Bob Suter, Mr. Suter 11 assigned to your division? 12 A. I recollect that Mr. Suter was 13 the senior HR support person for my 14 department, yes. 15 Q. Did he set up a meeting between 16 you and Mr. Krahling? 17 A. As I said, I don't recollect 18 having a specific discussion with Mr. Suter 19 about Mr. Krahling. So I obviously have no 20 specific recollection of such a meeting. 21 Q. Well, the question wasn't asked 22 about whether you had a conversation. You 23 said did he set it up. He could have set 24 it up by e-mail. 25 A. I don't recall.</p>

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1 Q. Did he make a recommendation to
 2 you that there be a meeting between you and
 3 Mr. Krahling?
 4 MS. DYKSTRA: Objection.
 5 THE WITNESS: Again, I do not
 6 recall.
 7 BY MR. BEGLEITER:
 8 Q. But you do recall there was a
 9 meeting --
 10 MS. DYKSTRA: Objection.
 11 BY MR. BEGLEITER:
 12 Q. -- with you and Mr. Krahling?
 13 A. Upon review of the documents
 14 there was a suggestion that there was a
 15 meeting, yes.
 16 Q. Which documents did you review
 17 that suggested that?
 18 A. There was -- if I remember
 19 correctly there was a document that was sent
 20 by -- to me by Mr. Suter actually. There was
 21 a notation on the document relating to the
 22 fact that Mr. Krahling had shown me, though I
 23 don't know who made the notation, it was a
 24 handwritten notation, Mr. Krahling had shown
 25 me data that caused him some concern.

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1 Q. Caused Mr. Suter some concern?
 2 A. Caused Mr. Krahling some concern.
 3 Q. Mr. Krahling. Okay.
 4 Do you recall what the category
 5 of data was?
 6 A. I do not recall the exact data
 7 that was -- or what was shown to me.
 8 Q. Was a meeting ultimately set up
 9 in your office?
 10 MS. DYKSTRA: Objection.
 11 THE WITNESS: Well, again, to my
 12 recollection, that was data that was
 13 shown to me, that was shown to me by
 14 Mr. Krahling. So this was the event
 15 that I was referring to earlier that
 16 then led to my contacting counsel.
 17 BY MR. BEGLEITER:
 18 Q. Was that meeting a scheduled
 19 meeting in the sense that it wasn't a
 20 surprise?
 21 MS. DYKSTRA: Objection. Form.
 22 THE WITNESS: I have no
 23 recollection. I don't have specific
 24 recollection.
 25 BY MR. BEGLEITER:

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1 Q. I mean, did he come to your
 2 office unannounced?
 3 A. I don't have specific
 4 recollection.
 5 Q. What did Mr. Krahling bring with
 6 him to the meeting?
 7 MS. DYKSTRA: Objection. Asked
 8 and answered.
 9 MR. BEGLEITER: No, he --
 10 BY MR. BEGLEITER:
 11 Q. Go ahead.
 12 A. Only what was noted on the note
 13 that I reviewed, right, that he showed me some
 14 information, some data. I don't remember the
 15 exact terminology. So, again, I have no
 16 specific recollection of the nature of what I
 17 was shown.
 18 Q. How long did this meeting take?
 19 A. I have no recollection of the
 20 meeting here, per se, so I can't tell you how
 21 long it took.
 22 Q. You don't recall the meeting but
 23 you're convinced that there was a meeting?
 24 A. Only because it is documented,
 25 the documents suggest that there was a meeting

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1 and it led to an event afterwards, a follow
 2 up.
 3 Q. Did the document contain your
 4 version of a meeting with Mr. Krah?
 5 A. This was a document sent to me,
 6 again if I recall correctly, from Mr. Suter.
 7 Again, since I have no clear recollection of
 8 the meeting or what was seen, my only
 9 recollection is, in quotes, my recollection in
 10 quotes is what is in the document.
 11 Q. And from that document does it
 12 appear that that document contains your
 13 version of what happened at that meeting?
 14 A. I don't recollect the meeting so
 15 the answer to the question is I don't know.
 16 Q. Whether you recollect the
 17 meeting or not is not my question. My
 18 question is whether or not did it appear to
 19 contain your version of what happened
 20 sometime. Maybe meeting is the wrong word.
 21 A. Well, it was Mr. Suter's version
 22 of it because -- but, again, this was a
 23 handwritten note on the side of this memo and
 24 I don't recall, nor am I certain that I really
 25 know who wrote that note.

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1 Q. What was the subject of the
 2 memo?
 3 MS. DYKSTRA: Objection. Form.
 4 THE WITNESS: I don't recall the
 5 exact subject of the memo. I do recall
 6 that it was also a heavily-redacted
 7 memo. So obviously there were other
 8 things in that there had nothing to do
 9 with mumps.
 10 BY MR. BEGLEITER:
 11 Q. So you can't recall if there's a
 12 meeting but there's a memo which talks
 13 about --
 14 A. There having been one.
 15 Q. -- there having been one. Okay.
 16 And did Mr. Krahling bring with him any
 17 counting sheets? I'm asking you --
 18 A. I don't recall.
 19 Q. Trying to refresh your memory.
 20 Did he bring with him any counting sheets?
 21 A. I don't recall.
 22 Q. Did he bring with you a mock
 23 control plate?
 24 A. I don't recall.
 25 Q. Did he bring with you any kind

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1 of cell plate?
 2 A. I don't recall.
 3 Q. Did Mr. Krahling ask you to
 4 examine the monolayer on the plate and tell
 5 him how many plaques he saw?
 6 A. I don't recall. This is
 7 17 years ago.
 8 Q. Do you recall what Mr. Krahling
 9 asserted that was -- do you recall what
 10 Mr. Krahling asserted that was going on in the
 11 lab which he thought was improper?
 12 MS. DYKSTRA: Objection. Asked
 13 and answered.
 14 THE WITNESS: I don't recall the
 15 details. But obviously whatever was
 16 asserted led me to bring it to the
 17 attention of counsel immediately
 18 thereafter.
 19 BY MR. BEGLEITER:
 20 Q. Was Mr. Suter in the -- did the
 21 memo that you saw indicate that Mr. Suter was
 22 in the room and overheard anything, any
 23 conversations between you and --
 24 A. Not that --
 25 Q. Let me finish. And

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1 Mr. Krahling?
 2 A. No.
 3 Q. In terms of temporal terms
 4 between the time of when you went to seek
 5 legal advice, we can fix -- can we fix the
 6 date on that? When did you seek legal advice?
 7 Again, I'm not asking for the legal advice. I
 8 want to know when you sought it.
 9 A. It was obviously immediately
 10 thereafter because the FDA inspection
 11 occurred, if I remember correctly, it was only
 12 roughly a week, maybe two weeks thereafter. I
 13 don't recall, so it was immediately
 14 thereafter. So my seeking of legal advice
 15 occurred between the time I spoke with
 16 Mr. Krahling and the time that the FDA
 17 inspection occurred. I suspect very strongly
 18 it occurred almost immediately after
 19 Mr. Krahling came to me.
 20 Q. Did you suspect that Mr. Krahling
 21 was the cause of the inspection?
 22 A. No. No. I mean, it -- did I
 23 make the connection at the time? No, I
 24 actually -- I remember very clearly in my own
 25 mind, this I remember clearly, not making that

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1 connection, interestingly enough.
 2 Q. You thought to yourself that
 3 this is not because of Stephen Krahling?
 4 MS. DYKSTRA: Objection. Say
 5 that again.
 6 BY MR. BEGLEITER:
 7 Q. I'm trying to accurately
 8 paraphrase what he said.
 9 A. I remember clearly. The thought
 10 may have occurred to me, although, you know,
 11 subsequent to that, but on that day that the
 12 agency inspector showed up, that did not cross
 13 my mind at that time. That was likely because
 14 I was very focused on the fact that an agency
 15 inspector had shown up, and we needed to get
 16 everybody together to do what needed to be
 17 done.
 18 Q. Before that date, how often in
 19 your career had there been an unannounced
 20 visit from the FDA?
 21 A. Well, it would not have happened
 22 to me because very rarely would a research
 23 laboratory have been put into a position of
 24 running the assay the way in which this was
 25 done.

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1 Q. I'm only asking about you.
 2 Prior to the unannounced visit on August 6,
 3 2001, how often had there been an unannounced
 4 visit to one of the labs under your
 5 supervision?
 6 A. Under my supervision?
 7 Q. Yes.
 8 A. Never before. This was the
 9 first time.
 10 Q. Was this a startling event for
 11 you?
 12 MS. DYKSTRA: Objection.
 13 THE WITNESS: Well, it was an
 14 event that one remembers. That event I
 15 remember clearly associated with that
 16 one. Whether it would be startling,
 17 probably not because unannounced FDA
 18 inspections of ongoing clinical studies
 19 and/or of ongoing production facilities
 20 are not unusual. It happens all the
 21 time because we had a laboratory under
 22 my supervision that was involved in the
 23 conduct of a clinical assay in support
 24 of a clinical study and having an
 25 unannounced inspection from the agency

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1 was startling only because the agency
 2 showed up unannounced, but it was not
 3 an unusual event, if that was your
 4 question.
 5 BY MR. BEGLEITER:
 6 Q. Had you ever been -- had any
 7 laboratory under your supervision ever before
 8 been accused by the FDA of changing data?
 9 MS. DYKSTRA: Objection.
 10 THE WITNESS: No. But it
 11 never -- the opportunity for such an
 12 accusation if it were ever to be made
 13 never existed, but it existed with
 14 regard to a Protocol 007 only because
 15 there was the laboratory actually
 16 running the assay.
 17 BY MR. BEGLEITER:
 18 Q. Which was a rare event. Who
 19 else would run the assay if not for the
 20 laboratory?
 21 A. It would be either an external
 22 testing laboratory or another testing
 23 laboratory within the facility or a testing
 24 laboratory responsible for clinical assays
 25 over in the manufacturing division for the

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1 studies that they supported. What was
 2 unusual, if you want to use that terminology,
 3 was the fact that we were running these
 4 clinical assays in a laboratory, Dr. Krah's
 5 laboratory, that was originally designed to
 6 support assay development, to support
 7 research. But unannounced -- going back to
 8 your previous question, unannounced agency
 9 inspections related to any product, product
 10 under development, product that was licensed
 11 and produced, happens all the time.
 12 Q. Let's go back a second. So it
 13 was unusual, to use a word I think you were
 14 using, for the lab that developed the assay to
 15 actually do the assay testing, conduct the
 16 assay?
 17 A. Normally that would not be the
 18 case, and as noted in one of the documents
 19 that you showed me earlier today, it was noted
 20 in there that normally we would have
 21 transferred the assay onto a testing
 22 laboratory.
 23 Q. Typically?
 24 A. Typically. Typically, usually.
 25 Q. We've already gone over why that

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1 wasn't done.
 2 A. We've gone over why that wasn't,
 3 because there was time pressures.
 4 Q. Did you see a lawyer after -- a
 5 Merck attorney, again I don't want to know
 6 what he told you or you told him, but with
 7 regard to the unannounced visit, unannounced
 8 inspection, did you seek advice?
 9 A. I do not recollect.
 10 Q. Let me be clear. Going back a
 11 second. You went to see a lawyer after you --
 12 after something happened with Steve Krahling,
 13 whether it was a meeting or something else,
 14 you're not sure. It was a meeting that is
 15 recorded?
 16 A. It's a meeting that's recorded.
 17 I don't recollect the specifics of the
 18 meeting.
 19 Q. Did you at that point -- again,
 20 before the announced visit, did you at that
 21 point consider terminating Mr. Krahling?
 22 A. Oh, I don't recollect at all
 23 having ever thought that at that point. The
 24 reason why I went to counsel was because in
 25 response to what Mr. Krahling presented to me,

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<p style="text-align: right;">Page 302</p> <p>1 and I felt that I should bring it to counsel. 2 I'm going to leave it at that. 3 MS. DYKSTRA: Just caution you 4 not to get into privilege. 5 MR. BEGLEITER: I'm not going to 6 ask him. 7 MS. DYKSTRA: I wasn't cautioning 8 you. I was cautioning the Doctor. 9 THE WITNESS: She was yelling at 10 me. 11 BY MR. BEGLEITER: 12 Q. Were you accompanied to counsel 13 by Dr. Krah or Dr. Shaw or did you go 14 yourself? 15 A. I don't recall the specifics. 16 Q. Did you discuss Mr. Krahling's 17 interaction with you with Dr. Krah? 18 A. Did I discuss -- with Dr. Krah. 19 I don't recall. 20 Q. How about with Dr. Shaw? 21 A. I do not recall the specifics. 22 I don't recall. I don't recall if I had the 23 meeting. I don't have the specifics of the 24 meeting. Again, it was 17 years ago. 25 Q. And do you recall -- I'd like to</p>	<p style="text-align: right;">Page 304</p> <p>1 A. That was reporting the second 2 meeting. 3 Q. Right. What do that -- 4 A. Or the second interaction. 5 Q. What do you recall that memo 6 said about what Mr. Krahling had told you? 7 A. Just what I said. There was a 8 handwritten notation on the memo. It was a 9 wholly redacted memo. It was a handwritten 10 notation, and I don't know who wrote the 11 notation. Again, just for clarity, I don't 12 know whether it was Mr. Suter or anybody else 13 who wrote the notation noting that 14 Mr. Krahling had showed me, if I remember -- 15 if I remember correctly, had showed me some 16 information that caused concern, or that was 17 concerning to Mr. Krahling. 18 Q. Was there, after the unannounced 19 inspection, did you commence any kind of 20 internal -- withdrawn. 21 After that unannounced inspection, 22 was there any internal investigation that was 23 conducted? 24 A. Well, we conducted a full audit 25 as noted in the response that went back to</p>
<p style="text-align: right;">Page 303</p> <p>1 just make sure I know exactly what words, as 2 best you can remember, what you have -- what 3 Mr. Krahling orally, in writing, whatever, 4 communicated to you about what was going on in 5 the lab. 6 MS. DYKSTRA: Objection. Asked 7 and answered. 8 THE WITNESS: Only by what was 9 in the memos that were shown me. There 10 was the original communication which, 11 as best as I can tell, was solely by 12 memo, whether it was by memo or by 13 e-mail, whatever the case happens to 14 be, in which Mr. Krahling referred 15 specifically to HR-related issues. It 16 was solely HR-related issues at that 17 point. And then sometime subsequent to 18 that, there was a subsequent meeting in 19 which whatever Mr. Krahling showed me, 20 and, again, I don't remember the 21 specifics of it, led me to approach 22 counsel. 23 BY MR. BEGLEITER: 24 Q. Does that memorandum that 25 Mr. Suter apparently put together --</p>	<p style="text-align: right;">Page 305</p> <p>1 CBER approximately 20 days later. These are 2 all standard procedures that one follows to 3 address the observations of the inspector. 4 And also oftentimes what one does is one goes 5 beyond that to say, okay, so this is what the 6 inspector saw, therefore, we will address what 7 the inspector specifically saw. What we will 8 also do is conduct a broader assessment to 9 make sure that even though the inspector 10 didn't shine a light on something else, that 11 everything else is also operating the way it's 12 supposed to operate. So it's not unusual to 13 do that. 14 Q. Was there a witness' interview? 15 MS. DYKSTRA: Objection. Form. 16 THE WITNESS: I was not involved 17 in the overall audit so I can't tell 18 you. 19 BY MR. BEGLEITER: 20 Q. I didn't ask you whether you 21 were involved. I asked you whether to your 22 knowledge -- 23 A. To my knowledge. 24 Q. To your knowledge were witnesses 25 interviewed?</p>

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1 A. I don't recollect.
 2 Q. Were you interviewed by anyone?
 3 A. I actually don't recollect.
 4 Q. Again, I'm not asking what was
 5 said to counsel. Wasn't what you said to
 6 counsel --
 7 A. No. You're talking about the
 8 post 483.
 9 Q. No. I'm talking -- well, what
 10 I'm asking -- I'm not going to ask what was
 11 said, but did your counsel interview you?
 12 A. I do --
 13 MS. DYKSTRA: Objection.
 14 THE WITNESS: But I don't recall.
 15 BY MR. BEGLEITER:
 16 Q. Did you ever advise Mr. Krahling
 17 not to call the FDA about any problems he had
 18 in the lab?
 19 A. Not to my recollection.
 20 MR. BEGLEITER: Take a break
 21 now, and then I think we can -- I'm
 22 trying to see if I can wind it up. I'm
 23 not promising.
 24 VIDEOGRAPHER: Time is now 4:53.
 25 We're going off the video record.

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1 - - -
 2 (A recess was taken.)
 3 - - -
 4 VIDEOGRAPHER: The time is now
 5 5:16. We're back on the video record.
 6 BY MR. BEGLEITER:
 7 Q. Doctor, during the assay, the
 8 PRN assay in Protocol 007, did Dr. Krah's lab
 9 find that there were lots of vaccine that were
 10 out of compliance with the label, if you
 11 remember?
 12 A. Not that I -- well, you have to
 13 define the word "compliance" for me.
 14 Q. Well, where the end expiry was
 15 below 4.3?
 16 A. I don't recall.
 17 Q. You said there were three arms
 18 of the test, right, 4.9, 4.0 and 3.7.
 19 A. That were being tested in the
 20 007 clinical trial, three potencies of the
 21 vaccine.
 22 Q. Did the lab find that any other
 23 lots were below 4.0?
 24 MS. DYKSTRA: Objection.
 25 THE WITNESS: The study 007 was

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1 not looking at individual lots. Sorry,
 2 I don't understand your question.
 3 BY MR. BEGLEITER:
 4 Q. There was a preliminary subset.
 5 Is that correct?
 6 A. There was an earlier subset
 7 looking at a subset of sera, yes.
 8 Q. And during the course of this
 9 test, was MMD, did MMD do its own testing to
 10 determine if there were lots that were below
 11 4.0?
 12 MS. DYKSTRA: Objection.
 13 THE WITNESS: My apologies, but
 14 you're talking about two different
 15 things here which is confusing the
 16 question.
 17 BY MR. BEGLEITER:
 18 Q. Make it simple. With regard to
 19 in the 2000-2001 period, did MMD, Merck
 20 Manufacturing Division, do any testing to see
 21 if any of the lots that had been sent down
 22 to -- for use had below 4.0, had a below 4.0
 23 spec?
 24 MS. DYKSTRA: Objection.
 25 THE WITNESS: I do not know of

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1 specific data from MMD. I would not
 2 have seen it and I don't know.
 3 BY MR. BEGLEITER:
 4 Q. Let's show it to you.
 5 - - -
 6 (Exhibit Emini-27, 2/26/01
 7 E-mail, 00549510 - 00549535, was marked
 8 for identification.)
 9 - - -
 10 BY MR. BEGLEITER:
 11 Q. I'd like to show you what's been
 12 marked as Merck 549510 through 549535.
 13 I'm actually going to ask you to
 14 focus on the very first paragraph under "Ed"
 15 on the first page.
 16 A. Okay.
 17 Q. And first of all, is this a
 18 document that you received in the usual course
 19 of your -- is this a document that you
 20 received in the usual course of your
 21 employment at Merck? Let me ask the question,
 22 is the document that you received in the usual
 23 course of your employment at Merck?
 24 A. Yes, it is.
 25 Q. And tell me, sir, in that first

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<p style="text-align: right;">Page 310</p> <p>1 paragraph, the first sentence, "We have been 2 assisting MMD in responding to CBER questions 3 re mumps end-expiry by performing an interim 4 analysis on 600 children participating in the 5 mumps end-expiry study (200 per group, studied 6 at mumps potencies of 4.9, 4.0 and 3.7)." 7 Do you see that? 8 A. Yes. 9 Q. That study, was that study part 10 of the Protocol 007? 11 A. Yes. 12 Q. Now, did that study in the 13 preliminary subset indicate that lots below 14 3.7 were not -- did not meet the requirements 15 of immunogenicity? 16 MS. DYKSTRA: Objection. 17 THE WITNESS: No, that is not 18 the result. The result is indicated 19 right here in the memo. It says in the 20 last paragraph on that first page, all 21 the way down at this bottom, it 22 describes the neut assays. It says, 23 "By the neutralization assays, ...and 24 end-expiry of 4.0...", remember this 25 was one of the three levels that were</p>	<p style="text-align: right;">Page 312</p> <p>1 BY MR. BEGLEITER: 2 Q. It then says -- 3 A. It then says, Jerry, that would 4 be Gerald Sadoff, and I feel 3.7 is medically 5 okay and would be defensible to the office of 6 compliance. And based on the data, I would 7 agree. 8 Q. The last sentence of that 9 paragraph under "Ed" it says, the last two 10 sentences, "The less than 3.7 lots are of 11 particular concern; the 3.7 to 4.0 lots are 12 likely defensible with some additional work." 13 And then it says, "All 106 lots are a 14 compliance issue." 15 Do you see that? 16 A. Right. So I don't know what 17 the -- I believe the 106 lots are referring to 18 the lots that they believe at end expiry may 19 be below. It's unclear from what's written 20 here. Maybe below that declared level which 21 the agency had declared at 4.3. The data, I'm 22 reading the penultimate sentence in the first 23 paragraph, the 3.7 to 4.0 lots are likely 24 defensible. And given the data at the end of 25 this page, I would agree, they are defensible</p>
<p style="text-align: right;">Page 311</p> <p>1 tested in 007, "...meets CBER's 2 demand...", as was noted here, CBER's 3 perspective criteria for 90 percent 4 seroconversion rate. So 4.0 is fine. 5 While the 3.7 log titer misses, right, 6 with 88.2 percent seroconversion rate 7 but a 95 percent confidence interval of 8 82.3 to 92.6. 9 Now, going back to our earlier 10 conversation from today, this is not an 11 assessment of efficacy. Rather what 12 this is, is a measure of the ability of 13 the vaccine at these three different 14 tested potency levels to elicit a 15 measurable immune response as measured 16 by the assay. CBER obviously placed a 17 criterion around what they would accept 18 as given the assay of an acceptable 19 seroconversion rate, criterion that was 20 established on the basis of, I'm not 21 exactly certain what, but they 22 established it at 90 percent, that 23 that's what they wanted to do, and they 24 did it. You will note that the 25 confidence interval crosses 90 percent.</p>	<p style="text-align: right;">Page 313</p> <p>1 because the data are not ostensibly different 2 between 4.0 and 3.7. 3 The reason why the 3.7 lots are 4 of particular concern, less than 3.7 lots are 5 of particular concern is that there are no 6 data on the level of seroconversion that would 7 be -- that would occur because the study only 8 went down to 3.7 lots, so what would happen at 9 3.5, 3.4, any lower number, there are no data. 10 So it's classic unknown lines. 11 Q. But there was data at 3.7 and 12 4.0. Is that correct? 13 A. Right there, yes. 14 Q. So I'm asking about the -- I'm 15 talking about the lots which were between 4.0 16 and 3.7. Those are the -- aren't those the 17 lots, 106 lots which are a compliance issue? 18 MS. DYKSTRA: Objection. 19 THE WITNESS: The wording is 20 unclear, but it may refer that -- those 21 106 lots may refer to those lots 22 between 3.7 and 4.0. 23 BY MR. BEGLEITER: 24 Q. You got this e-mail on 25 February 23, 2001?</p>

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<p style="text-align: right;">Page 314</p> <p>1 A. Okay. Yes.</p> <p>2 Q. And did you do anything about</p> <p>3 that after learning that 106 lots may be a</p> <p>4 compliant -- are a compliance issue?</p> <p>5 A. That is a matter of regulatory</p> <p>6 discussion between the company and CBER.</p> <p>7 There was nothing for me to do.</p> <p>8 Q. Do you know how many doses there</p> <p>9 are in 106 lots?</p> <p>10 A. I don't know how many doses are</p> <p>11 in a lot.</p> <p>12 Q. You weren't consulted on what to</p> <p>13 do with those 106 lots?</p> <p>14 MS. DYKSTRA: Objection.</p> <p>15 THE WITNESS: No, because I</p> <p>16 would not have been consulted. The</p> <p>17 data are very clear and I would not</p> <p>18 disagree with the conclusions here.</p> <p>19 The 106 lots, what we know from the 007</p> <p>20 data from the initial analyses that</p> <p>21 were done, is that at 3.7 the</p> <p>22 seroconversion rate has a confidence</p> <p>23 interval that crosses 90 percent. So</p> <p>24 statistically there is no difference in</p> <p>25 the seroconversion rate on a potency of</p>	<p style="text-align: right;">Page 316</p> <p>1 the end expiry number, and remember the</p> <p>2 number had been established by the</p> <p>3 agency at 4.3 initially simply because</p> <p>4 it was simply the number that was in</p> <p>5 the original label that you showed me</p> <p>6 this morning and therefore the agency</p> <p>7 said this should probably be the end</p> <p>8 expiry number, without there being any</p> <p>9 data supporting whether it should be</p> <p>10 that number or a lower number or for</p> <p>11 that matter a higher number, which is</p> <p>12 why the 007 was being conducted, in</p> <p>13 that sense a formal compliance</p> <p>14 accepting 4.3 as representative of the</p> <p>15 end expiry number which is the way the</p> <p>16 agency interpreted it in the initial</p> <p>17 communications, then by definition,</p> <p>18 they are these lots that are below 4.0,</p> <p>19 certainly below 4.3, are a potential</p> <p>20 compliance issue, but not a medical</p> <p>21 issue.</p> <p>22 BY MR. BEGLEITER:</p> <p>23 Q. If it was -- how do you know</p> <p>24 that? How do you know it's not a medical</p> <p>25 issue? How do you know what the consequences</p>
<p style="text-align: right;">Page 315</p> <p>1 4 or a potency of 3.7, which is why --</p> <p>2 which is why there was the statement</p> <p>3 here saying that Jerry, who was in</p> <p>4 medical at the time and Dorothy</p> <p>5 Margolskee together agreed that 3.7 is</p> <p>6 medically acceptable and defensible,</p> <p>7 and she says it twice.</p> <p>8 BY MR. BEGLEITER:</p> <p>9 Q. But I'm talking about the lots</p> <p>10 between 3.7 and 4.0.</p> <p>11 A. That's the one I'm talking</p> <p>12 about.</p> <p>13 Q. So there is no --</p> <p>14 A. There are only -- I'm sorry.</p> <p>15 Q. Do you know what the FDA was</p> <p>16 informed of this?</p> <p>17 MS. DYKSTRA: Objection.</p> <p>18 THE WITNESS: In continuous</p> <p>19 communications I don't know personally</p> <p>20 whether or not the agency was informed</p> <p>21 but these were the kinds of things we</p> <p>22 shared continuous communications</p> <p>23 between the agency and the company.</p> <p>24 And given that this was a question,</p> <p>25 existing question of where to establish</p>	<p style="text-align: right;">Page 317</p> <p>1 are -- withdrawn.</p> <p>2 How do you know what the</p> <p>3 conferences are of selling -- of using vaccine</p> <p>4 below 4.1?</p> <p>5 A. Look at the data right here. So</p> <p>6 what do we know. We know that the vaccine has</p> <p>7 retained field effectiveness. So we know the</p> <p>8 vaccine is effective even though there</p> <p>9 clearly, as is noted here, 106 lots that are</p> <p>10 between 3.7 and 4.0, with that number of lots</p> <p>11 with the number of doses probably involved in</p> <p>12 that number of lots, if this was ineffective</p> <p>13 vaccine, you would have had a large outbreak</p> <p>14 of mumps. It was never seen.</p> <p>15 So you have 106 lots that fall</p> <p>16 between 3.7 and 4.0 field effectiveness. The</p> <p>17 agency was clearly comfortable with that</p> <p>18 conclusion because 007 is based on the basis</p> <p>19 that the vaccine's effectiveness still exists.</p> <p>20 So now the question is where for control</p> <p>21 purposes do we put the end expiry number in</p> <p>22 the label.</p> <p>23 So they're using seroconversion</p> <p>24 as a surrogate measure of vaccines</p> <p>25 immunological potency. All the way down to</p>

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<p style="text-align: right;">Page 318</p> <p>1 3.7, so that would encompass these lots 2 obviously between 3.7 and 4.0. All the way 3 down to 3.7, the seroconversion, 95 percent 4 confidence interval gave a rate that is 5 statistically not different than the number 6 observed at four logs. 7 Q. If the label says 4.3, which it 8 did, we talked about that this morning. 9 A. Right. 10 Q. And at 4.0 to 3.7, there's an 11 understanding at Merck that these are -- 12 there's a compliance issue with regard to 13 those 106 lots. Right? 14 MS. DYKSTRA: Objection. 15 THE WITNESS: Relative to the 16 label. 17 BY MR. BEGLEITER: 18 Q. Yes, relative to the label. 19 A. Just be clear, compliance can 20 mean many things. 21 Q. So whether or not it's medically 22 or not medically a problem, let's assume it's 23 not medically -- 24 A. You -- 25 Q. It's probably medically, but...</p>	<p style="text-align: right;">Page 320</p> <p>1 don't know. 2 BY MR. BEGLEITER: 3 Q. Do you know that there have been 4 outbreaks over the last several years? 5 A. There have been, yes. But there 6 have been outbreaks of other vaccines related 7 to diseases as well. So there's nothing to 8 conclude. 9 Q. You were in favor of using 10 antihuman IgG in Protocol 007 AIGENT PRN. 11 Right? 12 A. That was a conclusion that was 13 drawn between the company and the agency. 14 Q. I'm talking about you. That was 15 the question. You were in favor of it? 16 MS. DYKSTRA: Objection. 17 THE WITNESS: I was in favor of 18 it because of the nature of what the 19 assay was being designed to do. And I 20 recollect that even prior to the review 21 of the documents, that the original 22 recommendation to use the anti-IgG 23 actually came from the agency. 24 BY MR. BEGLEITER: 25 Q. Do you know what document that</p>
<p style="text-align: right;">Page 319</p> <p>1 A. You can't say it's probably 2 medically, you don't know either. 3 Q. The lots were being sold as 4 being compliant with the label, weren't they? 5 MS. DYKSTRA: Objection. 6 THE WITNESS: The lots were 7 being sold, I cannot answer that 8 question whether or not the supposition 9 was that they were compliant with the 10 label or whether the vaccine was 11 considered to be effective. That is an 12 assessment that is made not just by the 13 company but by -- also by the FDA. The 14 FDA formally releases lots of the 15 vaccine. 16 BY MR. BEGLEITER: 17 Q. Let's move on to AIGENT. 18 You don't know what happened 19 with those 106 lots, do you? 20 A. I do not. 21 Q. Those 106 lots would have been 22 used in the late '90s or early 2000s. Is that 23 right? 24 MS. DYKSTRA: Objection. 25 THE WITNESS: Presumably, but I</p>	<p style="text-align: right;">Page 321</p> <p>1 is? 2 A. No, I just have a recollection 3 of the event, that the recommendation came 4 from the agency and within review of documents 5 I saw it as well, but I have an independent 6 recollection. 7 Q. Were you present when the agency 8 said it was okay to use AIGENT? 9 A. I cannot tell you under which 10 circumstance I was informed of that, but I do 11 recollect discussions that's where -- that 12 this was an agency-related recommendation. 13 Q. Sorry, that was a bad question. 14 I mean, were you present when the agency first 15 suggested that AIGENT be used? 16 MS. DYKSTRA: Objection. 17 THE WITNESS: That the anti-IgG 18 be used in the assay? 19 BY MR. BEGLEITER: 20 Q. Right. 21 A. I do not recollect the 22 circumstance. 23 Q. What was the purpose of using 24 antihuman IgG? 25 A. It is a general method to</p>

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<p style="text-align: right;">Page 322</p> <p>1 increase the sensitivity of a virus 2 neutralization assay when the virus 3 neutralization assay is designed to 4 specifically measure virus neutralizing 5 antibody. 6 Q. So it makes the testing more 7 sensitive, is that it? 8 A. It makes the testing more 9 sensitive. 10 Q. And is that a -- by adding the 11 antihuman IgG, is that an artificial way of 12 making the neutralization assays sensitive? 13 A. I will only answer that question 14 in the context of the definition of the word 15 artificial. The entire assay and all of its 16 components by definition are artificial to the 17 assay. 18 Q. How about very artificial? 19 MS. DYKSTRA: Objection. 20 THE WITNESS: That's a 21 non-answerable question. 22 MR. BEGLEITER: I'd like to show 23 you a document marked Bates numbers 24 549462 through 470. Have it marked 25 Exhibit 28.</p>	<p style="text-align: right;">Page 324</p> <p>1 Dorothy Margolskee? 2 A. Yes. 3 Q. So did she accurately relate 4 that in her discussion with you, that somehow 5 the neutralization assay is very artificial 6 because the IgG -- was the IgG added? 7 A. Well, very is a quantitative 8 term and I didn't write that, Dorothy 9 Margolskee wrote it, so I can't tell you what 10 the context in her mind was when she wrote it. 11 I will agree, as I said a moment ago, that the 12 assay, in all of its components is, 13 quote/unquote, artificial as it is designed to 14 measure only what it is designed to measure. 15 So what did I mean by that? 16 Q. Answer the question because I 17 was going to ask you that. 18 A. So this assay was designed to 19 measure virus neutralizing antibody. The 20 effort was made to conduct the assay in such a 21 way that would give rise to a high level of 22 sensitivity. So if you look at the three 23 different dose levels that were studied in the 24 007 study, the highest dose level was 4.9 25 logs, so this is well above even the 4.3 that</p>
<p style="text-align: right;">Page 323</p> <p>1 - - - 2 (Exhibit Emini-28, 2/26/01 3 E-mail with attachment, 00549462 - 4 00549470, was marked for identification.) 5 - - - 6 BY MR. BEGLEITER: 7 Q. I'm going to focus on a 8 paragraph on page 471, the bolded paragraph 9 towards the top. 10 A. Okay. 11 Q. Is this a document that you 12 received in the usual course of your 13 employment at Merck? 14 A. Yes, it is. 15 Q. Let me read the first sentence. 16 "In talking with Emilio, the neutralization 17 assay is very artificial because of the IgG 18 added; to avoid too many seropositives, very 19 high initial dilutions were required." Do you 20 think you're the Emilio referred to in this 21 sentence? 22 A. Since I was the only one with 23 that name at the company at the time, I 24 believe so, yes. 25 Q. So this is a document written by</p>	<p style="text-align: right;">Page 325</p> <p>1 was listed in the original label of the 2 vaccine. The reason why it was done at 4.9 3 logs was that the argument is made that we 4 know probably it's highly likely that this is 5 clearly an effective potency level for the 6 vaccine. Simply because going back to the 7 original studies that were done, the original 8 control studies done way back in 1960s with 9 the mumps vaccine, it was done at a potency 10 level, presumably at approximately 20,000, 11 because that's what came in the label. So 4.9 12 is above the 4.3, more than a half log above, 13 more than a half log above. 14 So, therefore, the argument is 15 we would like to have an assay that measures 16 seroconversion at the 90 percent level for at 17 least that 4.9 log level that's being tested, 18 right, because then we can benchmark what we 19 see at 4 and what we see at 3.7 using a very 20 sensitive assay. So the assay needed to be 21 designed to have a sensitivity of 90 percent. 22 Now, is what is being measured, 23 that immunological response that is being 24 measured, is that the actual immunological 25 basis for the vaccine's efficacy? That is not</p>

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<p style="text-align: right;">Page 326</p> <p>1 known. Even to this day it is not known. But 2 it is considered to be a surrogate measure of 3 the immunological response to the vaccine and, 4 therefore, a surrogate of effectiveness. But 5 remember it's a surrogate. True effectiveness 6 can only be established out in the field. So, 7 therefore, what was done under these 8 circumstances, the assays by definition is 9 artificial. 10 So what was the first thing that 11 was done? The first thing that was done was 12 to find a wild type strain that gave the 13 original assay a level that began to approach 14 90 percent. Hence the moving from the 15 London-1 strain to the low passage Jeryl Lynn 16 strain. So that was a change. It's designed 17 to change the assay to reflect a certain 18 biological response that you want to measure 19 at a given level. The addition of the 20 anti-IgG falls along the similar lines which 21 is an additional step that one put in to 22 enhance the likelihood that you would see that 23 virus neutralizing antibody responses. 24 So in the same sense that 25 switching to the low passage Jeryl Lynn strain</p>	<p style="text-align: right;">Page 328</p> <p>1 Q. Okay. And the way of making it 2 sensitive and the way of getting the results 3 that CBER was looking for was to add the 4 anti-IgG and use the wild type Jeryl Lynn? 5 MS. DYKSTRA: Objection. Form. 6 THE WITNESS: With their 7 concurrence because they wanted an 8 assay that was sufficiently sensitive 9 to distinguish among the three 10 different potency levels being tested 11 in 007. 12 BY MR. BEGLEITER: 13 Q. I'm going to show you three 14 documents, and the only purpose is for 15 authentication. Identify whether you received 16 these documents in the usual course of your 17 employment. I'm not going to ask you 18 substantive questions. 19 A. Yes. 20 - - - 21 (Exhibit Emini-29, E-mail 22 exchange, 00549497 & 00549498, was 23 marked for identification.) 24 - - - 25 MS. DYKSTRA: Do you want to</p>
<p style="text-align: right;">Page 327</p> <p>1 is artificial because it is a function of the 2 assay, the same thing is true for the addition 3 of the anti-IgG. 4 Q. So it's a way of -- so it's 5 another way of getting results that agree with 6 what's going on in the field. Is that what 7 you're saying? 8 A. It is another way of getting 9 results using, at a level of sensitivity that 10 would allow you to distinguish any differences 11 in the ability of the vaccine at the three 12 tested dose levels in 007 to elicit an 13 immunological response as measured by the 14 assay. 15 Q. So this was all the -- the two 16 things you're talking about, the wild type, 17 Jeryl Lynn being used over, let's say, the 18 London-1 and using antihuman IgG -- 19 A. Right. 20 Q. -- after the initial testing did 21 not meet what CBER was looking for? 22 MS. DYKSTRA: Objection. 23 THE WITNESS: In terms of 24 sensitivity. 25 BY MR. BEGLEITER:</p>	<p style="text-align: right;">Page 329</p> <p>1 give me all three, maybe I can 2 stipulate to the authenticity? 3 MR. BEGLEITER: Well, if you 4 give them back to me, I'm not going to 5 use it. I thought this was a document 6 that had your name on it. I apologize. 7 If you could give it back to me, I'd 8 appreciate it. 9 THE WITNESS: This one? 10 MR. BEGLEITER: Yeah. Oh, I 11 see. I see. 12 I'm sorry, we are going to use 13 it. We are going to use it, I'm sorry. 14 It's getting late in the afternoon. We 15 are going to use it. 16 BY MR. BEGLEITER: 17 Q. So I'd like you to take a look 18 at this, sir. Your name is not on it, but the 19 very first sentence -- this is, by the way, 20 document 549497 through 498. The first line 21 reads: I have given Emilio...60 cases -- 60 22 case numbers to re-test (the 42 failures plus 23 17 marginal positives). 24 MS. DYKSTRA: Can we have a 25 copy?</p>

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<p style="text-align: right;">Page 330</p> <p>1 BY MR. BEGLEITER: 2 Q. "I believe he will try to 3 re-test them with both ELISA (wild-type mumps) 4 and the wild-type neutral." [As read]. 5 Are you the Emilio referred to 6 here? 7 A. I believe I am, yes. 8 Q. Okay. Put it away. 9 I'm going to give the court 10 reporter Merck 68264 through 68271, ask her to 11 mark it, please. 30. 12 - - - 13 (Exhibit Emini-30, 11/10/00 14 E-mail with attachment, 00068264 - 15 00068271, was marked for identification.) 16 - - - 17 BY MR. BEGLEITER: 18 Q. Sir, I'm just going to ask you 19 on this document whether you received this in 20 the usual course of your employment? 21 A. Yes, I did. 22 Q. Put it away. 23 MR. BEGLEITER: If you guys give 24 me five minutes, one last look and see 25 if there's any more questions. Take a</p>	<p style="text-align: right;">Page 332</p> <p>1 submissions? 2 A. To the best of my recollection, 3 the auditing responsibility is either with 4 regulatory or a quality assurance group within 5 regulatory. 6 Q. And what does auditing require? 7 A. Auditing typically requires -- 8 any auditing typically requires that if you're 9 reporting on numbers or statements of fact, 10 that there are data, that there are actual 11 original data sources that you can trace to. 12 Q. Who is actually -- did you audit 13 submissions that Merck made to CBER about 14 Protocol 007? 15 A. Did I audit? 16 Q. Yes. 17 A. No, I would not audit it. No, 18 auditing is a very formal function. 19 Q. Did you ensure that quality 20 assurance audited Merck's submissions 21 regarding -- 22 A. I don't recollect -- sorry. I 23 don't recollect if I specifically requested 24 auditing for -- on quality assurance for CBER 25 submission, but that normally would have been</p>
<p style="text-align: right;">Page 331</p> <p>1 short break. 2 VIDEOGRAPHER: The time is 5:46. 3 Going off the record. 4 - - - 5 (A recess was taken.) 6 - - - 7 VIDEOGRAPHER: The time is now 8 5:50. We're back on the video record. 9 BY MR. BEGLEITER: 10 Q. Sir, isn't it true that every 11 submission that Merck sends to CBER must be 12 audited -- 13 MS. DYKSTRA: Objection. 14 BY MR. BEGLEITER: 15 Q. -- as far as you know? 16 A. As far as I know. That's 17 standard practice, yes, of course. 18 Q. Who is supposed to audit CBER 19 submissions? 20 MS. DYKSTRA: One second. I 21 don't think the Doctor has his 22 microphone on. 23 BY MR. BEGLEITER: 24 Q. Your voice carries. 25 Who is supposed to audit CBER</p>	<p style="text-align: right;">Page 333</p> <p>1 done by the regulatory group. 2 Q. Okay. So it was their prime 3 responsibility, the regulatory group, not 4 yours? 5 A. CBER submission is a regulatory 6 document and, therefore, it is the 7 responsibility of the regulatory group. 8 Q. Do you know if CBER was ever 9 sent audit results? 10 MS. DYKSTRA: Objection. 11 THE WITNESS: I would not know 12 that. 13 BY MR. BEGLEITER: 14 Q. Talking about with regard to 15 Protocol 007. 16 A. I am not aware. 17 Q. What state do you reside in? 18 A. The State of Pennsylvania. 19 Q. Do you plan on moving? 20 A. Not by tomorrow I'm not, no. I 21 mean, it's an open question. Do I ultimately 22 plan on moving? I don't know. 23 Q. I'm someone who doesn't like to 24 ask people's home address on a deposition. 25 MS. DYKSTRA: I will provide</p>

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<p style="text-align: right;">Page 334</p> <p>1 that to you if you need it. 2 MR. BEGLEITER: You'll agree to 3 provide it to me if I need it? 4 MS. DYKSTRA: If you need it. 5 MR. BEGLEITER: Thank you. I 6 have no further questions. 7 Your witness. 8 MS. DYKSTRA: Thank you. 9 - - - 10 EXAMINATION 11 - - - 12 BY MS. DYKSTRA: 13 Q. Dr. Emini, I just have a couple 14 of clarifying questions based on your 15 testimony today. 16 I'm going to mark as Emini-31, I 17 believe. 18 A. 31. 19 - - - 20 (Exhibit Emini-31, 12/1/99 21 Letter with attachment, 01201 - 01209, 22 was marked for identification.) 23 - - - 24 BY MS. DYKSTRA: 25 Q. Dr. Emini, do you recall -- this</p>	<p style="text-align: right;">Page 336</p> <p>1 different series that were tested. And for 2 the London-1 strain was approximately 3 69 percent when averaged across the two serum 4 series that were tested. 5 Q. What did Merck's practice, in 6 your experience, in connection with the 7 development of 007 for Merck to be candid and 8 transparent as it is here with the agency? 9 A. It was in my experience that 10 they were candid and transparent consistently 11 with the agency throughout all of the 12 discussions that we've been referencing today. 13 Q. You can put that document aside. 14 I'm going to ask you to pull 15 back Exhibit 6. It was already marked 16 Exhibit 6. Focus your attention on page 1, 17 which is -- Bates label on the bottom is 18 17043. Again, this is a March 12, 2001, 19 letter from Merck to CBER. Correct? 20 A. This is correct, yes. 21 Q. I just want to confirm, you had 22 received questions during your questioning 23 around the company's use of passage 8 of the 24 Jeryl Lynn strain. Do you recall that? 25 A. I don't have a specific</p>
<p style="text-align: right;">Page 335</p> <p>1 is a December 1, 1999, letter that Merck 2 submitted to CBER. Correct? 3 A. Yes. Yes, it is. 4 Q. Do you recall Mr. Begleiter 5 asked you whether or not Merck disclosed to 6 CBER the various seroconversion rates that 7 Merck had obtained using different strains 8 including the Lo1 strain of the virus? 9 A. Yes, I do. 10 Q. And if you look at page 2 of 11 this document, can you explain to me what is 12 referenced in the first paragraph that says, 13 "Merck's experience" and Table 2, the chart? 14 A. So the first paragraph refers to 15 a pilot study that was sera from children who 16 had been vaccinated with MMR II and assay, 17 with assays that were either using the Jeryl 18 Lynn strain, the low passage Jeryl Lynn strain 19 presumably and the London-1 strain as the 20 target strains in the assay. And initial 21 results of the experiments as stated and as 22 shown on Table 2 suggested that the measured 23 seroconversion rate using the Jeryl Lynn 24 strain was on average 91 percent. And you can 25 see the individual numbers here from the three</p>	<p style="text-align: right;">Page 337</p> <p>1 recollection of the discussion. 2 Q. Do you recall the discussions 3 with Mr. Begleiter? 4 A. Yes, I do, certainly. 5 Q. Do you recall he asked you about 6 the use of the anti-IgG? 7 A. Yes, I do. 8 Q. I just want to focus your 9 attention on the first paragraph of the CBER 10 submission. Let me know if this -- either you 11 can read this to us or tell us whether this 12 refreshes your recollection that Merck 13 confirmed with CBER, number one, that CBER 14 suggested the use of the anti-IgG, and that 15 CBER agreed to use passage 8 of the Jeryl Lynn 16 strain in 007. 17 A. The first paragraph states 18 clearly that "The newly developed 19 plaque-reduction neutralization assay...," 20 although you've been referring to it as the 21 PRN assay, "...using a wild-type mumps strains 22 has been optimized for use in the evaluation 23 of sera from the Mumps Expiry Trial...," this 24 is Protocol 007 as noted. Because the intent 25 was to use a sensitive assay for the reasons</p>

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<p style="text-align: right;">Page 338</p> <p>1 we discussed previously. 2 Assay description and the 3 standard operating protocol procedure was 4 submitted to CBER as background for the 5 November 29, 2000, conference. And as 6 suggested by CBER during the meeting held on 7 March 13th, the assay sensitivity for 8 measurement of virus neutralizing antibody has 9 been optimized by addition of the antihuman 10 IgG. It notes that the assay relies upon 11 immunostaining to reveal plaques since the 12 virus used in the assay is not ostensibly 13 cytopathic. And, therefore, also it's agreed 14 with CBER during the March 13, 2000, meeting 15 we have chosen the lowest available passage, 16 that would be passage 8. 17 MR. BEGLEITER: You're reading 18 very quickly. 19 THE WITNESS: It's verbatim -- 20 my apologies. I can read it again more 21 slowly. 22 So as I said, "As agreed with 23 CBER...", again, "...during the 24 March 13, 2000, meeting, we have chosen 25 the lowest available passage</p>	<p style="text-align: right;">Page 340</p> <p>1 Bennett and the second e-mail on the page is 2 from Keith Chirgwin. Do you have that in 3 front of you? 4 A. This one? 5 Q. Emini-11. 6 A. 11. 7 Q. Might be -- 8 A. No, no. It's just getting a 9 little confused here. My apologies. Yes, 11. 10 Q. So you -- do you recall -- 11 separate and apart from looking at the words 12 on this document, do you recall discussions 13 with Phil Bennett around his stability or any 14 stability modeling he may have done? 15 A. I do not have a specific 16 recollection of discussions with Phil Bennett. 17 Q. In the context of determining 18 whether shelf life of the vaccine should be, 19 how does the company determine that and what 20 would they rely on at this point in time -- 21 let me strike that. 22 You recall you had discussions 23 with Mr. Begleiter around CBER's 24 recommendation and approval to raise the 25 minimum release potency of the vaccine to 5.0</p>
<p style="text-align: right;">Page 339</p> <p>1 (passage 8) of the Jeryl Lynn strain of 2 mumps as being appropriately 3 representative of a wild-type mumps 4 virus strain." 5 BY MS. DYKSTRA: 6 Q. This paragraph in the submission 7 to CBER is consistent with your recollection 8 that CBER first suggested the use of antihuman 9 IgG and that they agreed that passage 8 of the 10 Jeryl Lynn strain was appropriate for this 11 assay? 12 A. It agrees with my recollection 13 of CBER's recommendation to use the antihuman 14 IgG to increase the sensitivity of the assay, 15 again, for the reasons we discussed 16 previously. And with regarding -- I did not 17 have a specific recollection of why the Jeryl 18 Lynn strain was chosen, but that was, 19 recollection occurred, if you will, as a 20 result of looking at documents over the past 21 several days. 22 Q. Thank you. I'm going to also go 23 back and ask you to look at what was marked 24 Emini Exhibit 11 today. This is a two-page 25 document from -- the first one is from Phil</p>	<p style="text-align: right;">Page 341</p> <p>1 log10 TCID50. Correct? 2 A. Yes, I do. 3 Q. In connection with that increase 4 in potency, what would the company do to 5 determine the appropriate shelf life of the 6 product? 7 A. Well, what would normally be 8 done in the context of an appropriate shelf 9 life is that one would conduct formal 10 stability studies which is, I believe, what I 11 answered before, formal stability studies that 12 would entail actual measurement of virus 13 potency at different time points in realtime 14 with in this case vaccine that had been stored 15 at the accepted storage temperature of the 16 vaccine, which is 28 degrees Celsius. 17 Q. So is that similar to saying 18 that the company would -- it would be 19 preferable or more reliable for the company to 20 rely on actual stability potency assay results 21 over time versus a stability model in 22 determining appropriate shelf life? 23 MR. BEGLEITER: Object to the 24 form. 25 THE WITNESS: Both the company</p>

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<p style="text-align: right;">Page 342</p> <p>1 and the agency, yes. 2 BY MS. DYKSTRA: 3 Q. Thank you. I wanted to just 4 clarify something that -- you had a question 5 during your examination around whether or not 6 you recall where the ELISA assay was 7 conducted. Dr. Krahl ran the PRN assay in your 8 building. Correct? 9 A. Yes, in his laboratory in my 10 building, in the building in which I had my 11 office, yes. 12 Q. Do you recall that Merck also 13 had a Wayne facility? 14 A. Yes, I do. 15 Q. Does that refresh your 16 recollection where the ELISA assay may have 17 been conducted? 18 A. Again, based on documents that I 19 was shown, yes, the Wayne facility by this 20 time had been put into place and ELISA assay 21 was performed there. The Wayne facility had 22 been put into place specifically to be a 23 physically separate facility for the conduct 24 of clinical assays, or assays in support of 25 clinical studies.</p>	<p style="text-align: right;">Page 344</p> <p>1 departing just for this, it's the AEO 2 document? Thank you. 3 BY MS. DYKSTRA: 4 Q. You said you thought they were 5 in quality assurance. Is that correct? 6 A. I believe. I don't have an 7 exact recollection. 8 Q. Can you just describe to me the 9 type of memos these are and whether or not 10 these are routine memos and the purpose of 11 this type of documentation of an FDA 12 inspection? 13 MR. BEGLEITER: Objection to the 14 form. 15 THE WITNESS: So these are 16 routine memos that are -- that refer, 17 that provide information and also to 18 the file of what transpired in 19 discussions that occurred during an FDA 20 inspection. 21 BY MS. DYKSTRA: 22 Q. And are they -- what is the 23 purpose of them, of these memos? 24 A. The purpose of these memos is to 25 provide a record of the nature of the</p>
<p style="text-align: right;">Page 343</p> <p>1 Q. If you could also pull back 2 Emini Exhibit 7. 3 A. Exhibit 7. 4 Q. It's an August 7, 2001, e-mail 5 from Karen McKenney which attaches the 483 and 6 a memo dated August 6, 2001, from Karen 7 McKenney, Kelly Pardue and Cathy Wadsworth. 8 A. Yes. 9 Q. I want to focus your attention 10 on the second two pages which are the memo 11 dated August 6, 2000, with the relined "FDA 12 Inspection of Virus and Cell Biology for Mumps 13 End Expiry Plaque Neutralization Assay." 14 A. Yes. 15 Q. Can you tell me, do you know who 16 the people on the "from" line are, McKenney, 17 Pardue and Wadsworth, what department they're 18 in? 19 A. I recall Cathy Wadsworth, I 20 believe that they were either in quality 21 assurance or somehow involved with regulatory, 22 but I'm not completely certain. 23 MS. DYKSTRA: Can I pause just 24 for a second? 25 Mr. Krahl, do you mind</p>	<p style="text-align: right;">Page 345</p> <p>1 discussions, to provide a record of specific 2 documents that were provided to the agency or 3 to the inspector at the inspector's request, 4 and to inform management of the relevant 5 personnel of the nature of what transpired. 6 Q. On the last page of the memo, it 7 says, "COPIES PROVIDED," and a list of 8 documents. Is that correct? 9 A. Yes. 10 Q. Would it be the responsibility 11 of the people in QA who prepare this memo to 12 include everything that was provided to the 13 FDA? 14 MR. BEGLEITER: Objection to 15 form. 16 THE WITNESS: It would be the 17 responsibility of whomever was asked. 18 What this memo indicates is that these 19 copies were provided, whether they came 20 directly from QA or they came from 21 someone else. But what the memo notes 22 is that all of these copies of these 23 documents were provided to the 24 inspector. 25 BY MS. DYKSTRA:</p>

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<p style="text-align: right;">Page 346</p> <p>1 Q. Just a couple of more documents 2 we'll look at briefly. If you can look at 3 Emini -- what was marked Emini Exhibit 8, 4 please. 5 A. Yes. 6 Q. That is an August 20, 2001, 7 letter from you to CBER in response or 8 following the August 6th inspection. Correct? 9 A. Correct. 10 Q. In this letter you have provided 11 answers, and I want to focus your attention on 12 page 1 of 3 under Observation number 1 which 13 is document Bates-labeled 482. 14 A. I'm sorry, the page notation, 15 yes. Thank you. 16 Q. And I want to focus your -- 17 MR. BEGLEITER: What page are 18 you on? 19 MS. DYKSTRA: I'm sorry. The 20 document labeled 482 at the bottom. 21 THE WITNESS: 482 at the bottom. 22 BY MS. DYKSTRA: 23 Q. I want to focus your attention 24 on one, two, the third paragraph which begins, 25 "We take seriously the issue of data integrity."</p>	<p style="text-align: right;">Page 348</p> <p>1 concern is that there may be an issue of data 2 integrity or not, so we conducted the set of 3 audits to show that that was not the case. 4 But on top of that, and this is routinely done 5 as well, which is to say let us make the 6 assumption that the corrections, that refers 7 to those corrections that were made without 8 justification, should not have been made. And 9 what if one analyzes the data using the 10 original uncorrected data. And what does one 11 get. Does one actually see a substantial 12 difference either one way or the other. And 13 what one is looking for, in fact, is a 14 difference that might in some way favor the 15 outcome of the study obviously. So that's 16 what one looks for. But as we're seeing here, 17 is that the overall seroconversion rates, in 18 fact, ostensibly didn't change. Overall 19 seroconversion rate on the analysis turned out 20 to be the original analysis with the 21 uncorrected data -- excuse me, with the 22 corrected data, the original analysis resulted 23 in the 92 percent seroconversion rate with a 24 95 percent confidence interval as noted 25 between 89.6 percent and 94.3 percent. By</p>
<p style="text-align: right;">Page 347</p> <p>1 A. Yes. 2 Q. You recall Mr. Begleiter asked 3 you about Dr. Krah's and/or anyone else's 4 counting or recounting of the assay plates in 5 the PRN assay. Do you recall those questions? 6 A. Yes, I do. 7 Q. In this statement to the agency 8 you relate an assessment of the uncorrected 9 and corrected results. Do you see that? 10 A. Yes, I do. 11 Q. Can you explain to me what this 12 paragraph means and how you interpret this or 13 what you recall of it? 14 A. Well, the correction as referred 15 to here would have been the correction that 16 was noted by the inspector when the 483 was 17 issued, the first observation of the 18 inspector, that there were some data numbers 19 that had been corrected but without there 20 being a written justification for the 21 correction. So that obviously opens the 22 question as to why this was done and why was 23 the correction made. 24 So part of the answer here, of 25 course, is that, you know, obviously one's</p>	<p style="text-align: right;">Page 349</p> <p>1 reanalysis where one goes back to the original 2 numbers, the overall seroconversion rate was 3 92.6 percent with a confidence interval of 4 90.2 percent to 95.1 percent. So what that 5 indicates, given the significant overlap 6 between -- among the two confidence intervals 7 is that whatever changes were made and 8 whatever the basis was, because it wasn't 9 noted, did not change the results. If 10 anything, if one was looking to potentially 11 raise the seroconversion level to a higher 12 number, the effect of the corrections which 13 were made which were not justified in the 14 document actually lowered the seroconversion 15 numbers. 16 MS. DYKSTRA: I'm going to mark 17 two more documents. I believe we're on 18 Emini-32. 19 - - - 20 (Exhibit Emini-32, 10/10/01 21 Letter, 01631027, was marked for 22 identification.) 23 - - - 24 BY MS. DYKSTRA: 25 Q. Dr. Emini, if you can look at</p>

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<p style="text-align: right;">Page 350</p> <p>1 what's been marked as Emini-32, which is an 2 October 10, 2001, letter from Manal Morsy to 3 Cathy Carbone at CBER, Bates-labeled 1631027. 4 I want to ask you whether or not, number one, 5 this refreshes your recollection with respect 6 to your questioning today around Dr. Ward at 7 all and/or -- just ask that. 8 Does this refresh your 9 recollection, this document with respect to 10 what Dr. Ward's lab -- what role Dr. Ward's 11 lab had in connection with 007? 12 A. According to this memo, the only 13 immediate connection was that, as Dr. Shaw 14 explained in the reading now, the one, two, 15 three, four, fifth paragraph down, Dr. Shaw 16 explained that the only positive and negative 17 controls sera samples were provided to 18 Dr. Ward. So these would typically be the 19 samples that would be provided to do an 20 initial assessment of the quality of the data 21 from the laboratory to determine whether or 22 not the results that Dr. Ward would obtain 23 would be similar to the results that were 24 obtained in the Merck laboratory. And as he 25 notes, the results for the control samples,</p>	<p style="text-align: right;">Page 352</p> <p>1 study? 2 A. Known negative samples and known 3 positive samples, yes. 4 Q. And known negative and known 5 positive mean what? 6 A. These are samples where you know 7 that the known negatives do not contain the 8 antibody that you're measuring. They're known 9 to that because you've assayed them many times 10 in different tests. The known positive 11 samples are samples from individuals who have 12 a range of antibody responses to what you're 13 measuring, which in this case is the mumps 14 virus. 15 Q. And known meaning based on other 16 assays, not Protocol 007? 17 A. Based on other assays. It is 18 known that they should register as positive. 19 The objective of the doing the study is to see 20 what number came out and to correlate that 21 number with the numbers obtained between the 22 two laboratories of Dr. Ward's and the 23 company. 24 Q. I'm going to show you one last 25 document which I've marked as Emini-33.</p>
<p style="text-align: right;">Page 351</p> <p>1 which is what those were, are consistent with 2 the Merck results. Dr. Shaw explained that 3 all the raw data from Mr. Ward's laboratory 4 had been provided to Ms. Debra Bennett from 5 the agency during her last visit to the 6 research laboratories, and the specific data 7 were given the geometric mean titers for the 8 two sera representing high and low value are 9 contained in the validation report which was 10 also previously supplied to CBER. 11 We believe this was probably, I 12 believe, I believe that this was probably in 13 response to a question from the agency as to 14 whether or not there were potential or 15 significant differences between the values 16 that would have been generated in Dr. Ward's 17 laboratory as opposed to the Merck laboratory, 18 Dr. Krah's laboratory and the results of the 19 data that were presented or submitted to the 20 agency is that that was not the case. 21 Q. The serum samples -- the sera 22 samples that were provided to Dr. Ward's lab 23 were not the 007 clinical sera samples, but 24 control samples used to, I guess, validate the 25 lab prior to actually running the clinical</p>	<p style="text-align: right;">Page 353</p> <p>1 - - - 2 (Exhibit Emini-33, 4/8/01 3 Letter, 0000328 - 0000331, was marked 4 for identification.) 5 - - - 6 BY MS. DYKSTRA: 7 Q. It's a little bit lengthy, 8 April 8, 2001, it looks like a letter to you 9 signed by on page 4 Stephen Krahling, 10 Bates-labeled RELATOR_000033 looks like 8 -- 11 328, 329, 330, 331. Can you take a look at 12 this and let me know what you recall, if 13 anything about this document or generally 14 about Mr. Krahling's complaints to you 15 regarding HR issues in Dr. Krah's lab? 16 A. So this is the document that I 17 reviewed prior to today and that I believe 18 referred to in my previous testimony that had 19 been shown to me and by which I recall that I 20 did, in fact, receive this document from 21 Mr. Krahling in which Mr. Krahling documented 22 rather extensively his perspective that the, 23 call it, the HR environment within Dr. Krah's 24 laboratory was, in fact, in his opinion 25 problematic.</p>

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<p style="text-align: right;">Page 354</p> <p>1 Q. And I see in the second 2 paragraph he comments around highly personal 3 relationships with female employees and 4 personal gifts. Do you see that? 5 A. Yes, I do. 6 Q. And in the third paragraph he 7 raises issues around work schedules. Do you 8 see that? 9 A. Yes. 10 Q. And in the last paragraph, 11 again, no vacation mandates and schedules? 12 A. Yes. 13 Q. And we can go forward in the 14 other paragraphs, just confirm that they also 15 raise other HR-type concerns? 16 A. All are HR environmental issues 17 yes. 18 Q. Do you recall -- strike that. 19 You noted that you had seen a 20 document that reflected that you met at some 21 point in time just prior to the agency's FDA 22 483 inspection in August 2001, that you had 23 met with Mr. Krahlung where he raised an 24 allegation of something different than HR, 25 something of concern to him?</p>	<p style="text-align: right;">Page 356</p> <p>1 complaint at the end of July, that you would 2 have contacted counsel? 3 MR. BEGLEITER: Objection to the 4 form. 5 THE WITNESS: As evidenced by my 6 action that I took in contacting 7 counsel after the meeting that I had 8 with Mr. Krahlung in which he showed me 9 his concerns over the data, the answer 10 to your question would be yes. 11 BY MS. DYKSTRA: 12 Q. But other than that meeting, you 13 don't have any recollection of Mr. Krahlung 14 raising to you anything other than HR 15 concerns? 16 A. I do not. 17 MS. DYKSTRA: I have no further 18 questions. 19 MR. BEGLEITER: Can you give me 20 a few minutes? 21 MS. DYKSTRA: Sure. 22 VIDEOGRAPHER: The time is 6:16. 23 Going off the video record. 24 - - - 25 (A recess was taken.)</p>
<p style="text-align: right;">Page 355</p> <p>1 A. Yes. 2 Q. You don't remember specifically 3 that meeting, but you remember seeing a 4 document that referenced that meeting? 5 A. That was a note from Mr. Suter 6 to me from HR. 7 Q. When you had that meeting 8 referenced in that document with Mr. Krahlung, 9 you stated that you immediately contacted 10 counsel. 11 A. Yes. 12 Q. Correct? 13 A. Yes. 14 Q. Other than that meeting that was 15 referenced in the document where you contacted 16 counsel, did Mr. Krahlung ever raise to you 17 any concerns regarding any fraud or 18 misconduct, I'm distinguishing that from HR 19 complaints, about the running of protocol in 20 any way? 21 A. Not to my recollection. 22 Q. Had he raised the complaint 23 around misconduct in the lab at any point in 24 time, is it fair to say that you would have 25 done just what you did when he raised his</p>	<p style="text-align: right;">Page 357</p> <p>1 - - - 2 VIDEOGRAPHER: The time is now 3 6:37. This begins tape six. 4 - - - 5 FURTHER EXAMINATION 6 - - - 7 BY MR. BEGLEITER: 8 Q. Doctor, I'd like you to turn 9 back to Exhibit 6, page 17043. 10 A. 43. 11 Q. Yes. Actually if you go -- 12 17043. Do you know who wrote paragraph A that 13 you read from? 14 A. Who physically wrote it? No, I 15 do not. 16 Q. It says here, "As suggested by 17 CBER during the meeting held on March 13, 18 2000, the assay's sensitivity for measurement 19 of virus-neutralizing antibody has been 20 optimized by addition of anti-human IgG." 21 A. Yes. 22 Q. So my question is, do you know 23 independent of this paragraph who at CBER made 24 that suggestion supposedly? 25 A. No, I do not.</p>

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<p style="text-align: right;">Page 358</p> <p>1 Q. Do you know whether CBER agrees 2 with the sentence? 3 MS. DYKSTRA: Objection. 4 THE WITNESS: Well, it was 5 CBER's suggestion and recommendation, 6 and then discussions were held 7 continuously with CBER. So CBER was 8 certainly aware that this was 9 happening, and if they had a 10 suggestion, they would have entered it. 11 BY MR. BEGLEITER: 12 Q. Doctor, my question is, did you 13 know if the person who wrote this got it 14 right? 15 MS. DYKSTRA: Objection. 16 THE WITNESS: By definition I 17 cannot know that. 18 BY MR. BEGLEITER: 19 Q. Thank you. 20 A. By definition. 21 Q. Let's go to Exhibit 31. That's 22 the document you used to discuss the London-1 23 isolate? 24 A. Yes. 25 Q. Do you know at what potencies</p>	<p style="text-align: right;">Page 360</p> <p>1 withdrawn. Let me just go on to the next one. 2 Let's go to Exhibit 32. Do you 3 have that in front of you? 4 A. Yes, I do. Yes. 5 Q. Is there anything in this letter 6 which explains to you why Dr. Ward's lab was 7 not used for Protocol 007? 8 A. No, that was not the intent of 9 this letter. 10 Q. How do you know what the intent 11 was? 12 A. Well, because -- I am inferring 13 the intent of this letter because what is 14 being reported here is that using the control 15 sera, the data from Dr. Ward's laboratory were 16 identical and were comparable, I'm looking for 17 the exact word that was used here, to the data 18 from the Merck laboratory are consistent with 19 the Merck results was the terminology that was 20 used. So the intent here presumably was to 21 show that the two assays, you know, could be 22 consistent. This was not a validation study, 23 this was just simply a determination looking 24 for consistency. 25 Q. So this would be a reason to</p>
<p style="text-align: right;">Page 359</p> <p>1 the London-1 isolate was tested at? 2 MS. DYKSTRA: Objection. 3 THE WITNESS: Please define 4 "potency." 5 BY MR. BEGLEITER: 6 Q. If you don't understand the word 7 potency, I'm just going to go on to the next 8 question. You don't know what the word 9 "potency" means? 10 A. I don't know what the potency 11 means in context of your question. You said 12 at what potencies was it tested, are you 13 referring to the potency -- 14 Q. In other words -- I understand. 15 The 007 data was testing at three potencies, 16 were they not? 17 A. At three potency levels, yes. 18 In the context of 007 study, yes. No, I do 19 not -- so to answer your question -- 20 Q. You do not know? 21 A. I do not know because I do not 22 know what the serum series specifically refer 23 to. 24 Q. So you can't tell whether or not 25 London-1 here was subject to the same --</p>	<p style="text-align: right;">Page 361</p> <p>1 corroborate the use of Dr. Ward's lab, 2 wouldn't it? 3 MS. DYKSTRA: Objection. 4 THE WITNESS: It would be a 5 reason for stating that if one wanted 6 to -- well, no, again, this was not a 7 formal validation. That would depend 8 on the validation of the assay in 9 Dr. Ward's laboratory, and it would 10 depend on the actual validation of the 11 laboratory itself. 12 BY MR. BEGLEITER: 13 Q. There are reasons why it 14 would -- why you could or you couldn't, but 15 I'm saying this letter isn't a negative to 16 using Dr. Ward's lab? 17 A. No, it is not directly a 18 negative. 19 Q. Directly a negative? 20 A. Directly a negative. 21 Q. What do you mean "directly a 22 negative"? 23 A. I'm sorry, directly meaning it 24 does not directly state don't use it or the 25 data don't directly state you cannot use it.</p>

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1 Q. Let's go to Exhibit 8. With
 2 regard to 007, sir, do you know -- do you have
 3 a definition of pre-positive?
 4 A. Sorry, are you reading in a
 5 specific place?
 6 Q. I'm not reading anything.
 7 A. Just a question, sorry. You
 8 said Exhibit 8, my apologies. A definition of
 9 a pre-positive?
 10 Q. Yes.
 11 A. So my definition of a
 12 pre-positive would be a serum sample from
 13 someone who had not received the vaccine or
 14 had not been exposed to the virus in the
 15 course of natural infection.
 16 Q. Does pre-positive imply that
 17 there is some, for example, some plaques in a
 18 cell plate that just a small number of plaques
 19 before -- withdrawn.
 20 Does it imply that there are
 21 some plaques in a cell plate before the
 22 subject has -- before mumps has been
 23 introduced into the plate?
 24 A. The plaques in a cell plate are
 25 a function of the indicator virus that one

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1 places in the cell plate. It does not refer
 2 to the pre-positive sample, per se.
 3 Q. So pre-positive would be a
 4 sample in which the child in this case would
 5 not have -- did not have mumps?
 6 MS. DYKSTRA: I'm going to
 7 object because this is beyond the
 8 direct examination.
 9 MR. BEGLEITER: This is exactly
 10 what it's going to.
 11 MS. DYKSTRA: Well, it doesn't
 12 seem like it's going to, because I
 13 didn't talk about pre-positive. So
 14 I'll give you a little bit of latitude,
 15 but then I'm going to object.
 16 MR. BEGLEITER: You can object,
 17 but it relates to this on page on
 18 Exhibit 8. So that's exactly where I'm
 19 going to. I'm asking a foundation
 20 question.
 21 BY MR. BEGLEITER:
 22 Q. So my question, again, is, make
 23 sure we understand it, a pre-positive is one
 24 where someone would look at the cell plate and
 25 exclude it from the study because it was

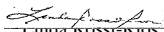
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1 pre-positive. Isn't that right?
 2 MS. DYKSTRA: Objection. Form.
 3 THE WITNESS: So the use of the
 4 terminology pre-positive in that
 5 regard, that is referring to an
 6 individual who you believe not to have
 7 been vaccinated, no record of
 8 vaccination or no record of natural
 9 exposure to the virus and yet when the
 10 assay is run, there was an indication
 11 of antibody, plaque reduction
 12 neutralizing antibody present.
 13 BY MR. BEGLEITER:
 14 Q. Okay. And the pre-positives are
 15 usually excluded from the testing. Isn't that
 16 right?
 17 MS. DYKSTRA: Objection.
 18 THE WITNESS: It would depend on
 19 the level of the pre-positivity. If
 20 you had such a pre-positive, you would
 21 not be able, using the assay, to
 22 discern whether or not the individual
 23 seroconverted subsequent to
 24 immunization because there was already
 25 antibody apparently present prior to

Page 365

1 immunization.
 2 BY MR. BEGLEITER:
 3 Q. Let's go back to Exhibit 8.
 4 I'll ask you whether or not there was any
 5 indication here that pre-positives were
 6 considered in coming to the conclusions that
 7 were come to?
 8 MS. DYKSTRA: Are you referring
 9 just to the paragraph?
 10 MR. BEGLEITER: The paragraph
 11 that you read on page 482.
 12 THE WITNESS: I'll read it
 13 again. There is no indication given
 14 what is stated in this paragraph that
 15 there were any considerations one way
 16 or the other related to the concept of
 17 pre-positivity.
 18 BY MR. BEGLEITER:
 19 Q. What would be the impact of
 20 pre-positive on the corrections that were
 21 related in this paragraph?
 22 MS. DYKSTRA: Objection. Form.
 23 THE WITNESS: I can't answer
 24 that question because it would depend
 25 on what samples were individually

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<p style="text-align: right;">Page 366</p> <p>1 corrected and what the nature of that 2 correction was and what that entailed, 3 so I can't answer the question. I 4 don't know. 5 BY MR. BEGLEITER: 6 Q. Did you tell CBER of the impact 7 on pre-positives? 8 MS. DYKSTRA: Objection. Form. 9 THE WITNESS: I was not directly 10 involved with any discussions with CBER 11 around that question. 12 BY MR. BEGLEITER: 13 Q. Who did this reanalysis that's 14 mentioned in this paragraph? 15 A. This reanalysis was performed by 16 the statistical group, as it would have been 17 performed. 18 Q. So they didn't have the cell 19 plates in front of them? 20 MS. DYKSTRA: Objection. 21 THE WITNESS: What they had in 22 front them were the two sets of data, 23 the original so-called uncorrected data 24 and then the subsequent corrected data. 25 BY MR. BEGLEITER:</p>	<p style="text-align: right;">Page 368</p> <p>1 A. That would be the manufacturing 2 division and the marketing division, not us. 3 MR. BEGLEITER: Thank you. 4 Thank you, Doctor. 5 MS. DYKSTRA: Thank you. 6 VIDEOGRAPHER: The time is 6:48. 7 This concludes the deposition of Emilio 8 Emini. 9 - - - 10 (Witness excused.) 11 - - - 12 (Deposition concluded at 13 6:48 p.m.) 14 15 16 17 18 19 20 21 22 23 24 25</p>
<p style="text-align: right;">Page 367</p> <p>1 Q. What this paragraph relies on is 2 the integrity of that data? 3 A. What this relies on are -- well, 4 all analyses rely on the integrity of data by 5 definition, yes. 6 Q. On Exhibit 8, again, did -- was 7 there ever a point at which undiluted IgG was 8 added to the PRN test for Protocol 007? 9 MS. DYKSTRA: Objection. 10 THE WITNESS: I have no way of 11 knowing that. 12 BY MR. BEGLEITER: 13 Q. You don't know? 14 A. I don't know. 15 Q. I do have a question, it's a 16 follow up for today. Just one question. It's 17 a yes or a no. 18 Is there a way for Merck to 19 determine who purchased 106 out of compliance 20 lots? 21 MS. DYKSTRA: Objection. Form. 22 THE WITNESS: I would not know 23 if there is a direct way of doing that. 24 BY MR. BEGLEITER: 25 Q. That would be --</p>	<p style="text-align: right;">Page 369</p> <p>1 CERTIFICATE 2 3 4 I do hereby certify that I am a Notary 5 Public in good standing, that the aforesaid 6 testimony was taken before me, pursuant to 7 notice, at the time and place indicated; that 8 said deponent was by me duly sworn to tell the 9 truth, the whole truth, and nothing but the 10 truth; that the testimony of said deponent was 11 correctly recorded in machine shorthand by me 12 and thereafter transcribed under my 13 supervision with computer-aided transcription; 14 that the deposition is a true and correct 15 record of the testimony given by the witness; 16 and that I am neither of counsel nor kin to 17 any party in said action, nor interested in 18 the outcome thereof. 19 20 WITNESS my hand and official seal this 21 19th day of June, 2017. 22 23 24 25</p> <p style="text-align: center;">  Emilio Kossis-Christos, RPR, CSR Notary Public </p>

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<p style="text-align: right;">Page 370</p> <p>1 INSTRUCTIONS TO WITNESS</p> <p>2 Please read your deposition over</p> <p>3 carefully and make any necessary corrections.</p> <p>4 You should state the reason in the appropriate</p> <p>5 space on the errata sheet for any corrections</p> <p>6 that are made.</p> <p>7 After doing so, please sign the errata</p> <p>8 sheet and date it.</p> <p>9 You are signing same subject to the</p> <p>10 changes you have noted on the errata sheet,</p> <p>11 which will be attached to your deposition.</p> <p>12 It is imperative that you return the</p> <p>13 original errata sheet to the deposing attorney</p> <p>14 within thirty (30) days of receipt of the</p> <p>15 deposition transcript by you. If you fail to</p> <p>16 do so, the deposition transcript may be deemed</p> <p>17 to be accurate and may be used in court.</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 372</p> <p>1 ERRATA SHEET</p> <p>2 IN RE: USA ex rel. vs. MERCK</p> <p>3 DATE: 6/6/2017</p> <p>4 PAGE LINE CORRECTION AND REASON</p> <p>5 _____</p> <p>6 _____</p> <p>7 _____</p> <p>8 _____</p> <p>9 _____</p> <p>10 _____</p> <p>11 _____</p> <p>12 _____</p> <p>13 _____</p> <p>14 _____</p> <p>15 _____</p> <p>16 _____</p> <p>17 _____</p> <p>18 _____</p> <p>19 _____</p> <p>20 _____</p> <p>21 _____</p> <p>22 _____</p> <p>23 _____</p> <p>24 _____</p> <p>25 (DATE) DR. EMILIO EMINI</p>
<p style="text-align: right;">Page 371</p> <p>1 ACKNOWLEDGMENT OF DEPONENT</p> <p>2</p> <p>3 I have read the foregoing transcript of</p> <p>4 my deposition and except for any corrections or</p> <p>5 changes noted on the errata sheet, I hereby</p> <p>6 subscribe to the transcript as an accurate record</p> <p>7 of the statements made by me.</p> <p>8</p> <p>9 _____</p> <p>10 DR. EMILIO EMINI</p> <p>11</p> <p>12 SUBSCRIBED AND SWORN before and to me</p> <p>13 this ____ day of _____, 20__.</p> <p>14</p> <p>15</p> <p>16 _____</p> <p>17 NOTARY PUBLIC</p> <p>18</p> <p>19</p> <p>20 My Commission expires:</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	

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10/25/2019
Declaration of G. Reilly
EXHIBIT 116

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA : CIVIL ACTION
ex rel., STEPHEN A. : NO. 2:10-04374 (CDJ)
KRAHLING and JOAN A. :
WLOCHOWSKI, :
Plaintiffs, :
vs. :
MERCK & CO., INC., :
Defendant. :

_____ : Master File No.
IN RE: MERCK MUMPS : 2:12-cv-03555 (CDJ)
VACCINE ANTITRUST :
LITIGATION :

THIS DOCUMENT RELATES TO: :
ALL ACTIONS :

** CONFIDENTIAL **

December 22, 2016

Videotaped deposition of FLORIAN
SCHODEL, MD, taken at the offices of Spector
Roseman Kodroff & Willis, 1818 Market Street,
Suite 2500, Philadelphia, Pennsylvania 19103,
beginning at 9:05 a.m., before LINDA
ROSSI-RIOS, a Federally Approved RPR, CCR and
Notary Public.

<p style="text-align: right;">Page 2</p> <p>1 APPEARANCES :</p> <p>2</p> <p>3 On behalf of the Plaintiffs:</p> <p>4 SPECTOR ROSEMAN KODROFF & WILLIS, P.C. BY: JOHN A. MACORETTA, ESQUIRE</p> <p>5 and DIANA J. ZINSER, ESQUIRE</p> <p>6 1818 Market Street Suite 2500</p> <p>7 Philadelphia, PA 19103 215.496.0300</p> <p>8 jmacoretta@srkw-law.com dzinser@srkw-law.com</p> <p>9</p> <p>10</p> <p>11 KELLER GROVER LLP BY: JEFFREY F. KELLER, ESQUIRE 1965 Market Street</p> <p>12 San Francisco, CA 94103 415.543.1305</p> <p>13 jfkeller@kellergrover.com</p> <p>14</p> <p>15 CONSTANTINE CANNON BY: ROBERT L. BEGLEITER, ESQUIRE 16 (Via teleconference) 335 Madison Avenue 17 New York, NY 10017 212.350.2707</p> <p>18 rbegleiter@constantinecannon.com</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 4</p> <p>1 I N D E X</p> <p>2</p> <p>3 WITNESS PAGE</p> <p>4 FLORIAN SCHODEL, MD</p> <p>5 By Mr. Keller 9</p> <p>6 By Mr. Macoretta 371</p> <p>7</p> <p>8 E X H I B I T S</p> <p>9 MARKED DESCRIPTION PAGE</p> <p>10 Schodel-1 Curriculum Vitae 24</p> <p>11 Schodel-2 LinkedIn profile 26</p> <p>12 Schodel-3 Immunological Correlates of Vaccine-Derived Protection Fondation Mérieux Conference Center 'Les Pensières' Veyrier-Du-Lac, France article 122</p> <p>13</p> <p>14</p> <p>15 Schodel-4 E-mail string, MRK-KRA01648951 - 1648956 129</p> <p>16</p> <p>17 Schodel-5 2/23/01 E-mail with attachment, MRK-KRA00549510 - 549535 153</p> <p>18</p> <p>19 Schodel-6 E-mail chain, MRK-KRA00549497 & 549498 206</p> <p>20</p> <p>21 Schodel-7 3/1/01 E-mail, MRK-KRA00549218 & 549219 220</p> <p>22</p> <p>23 Schodel-8 PowerPoint presentation, MRK-CHA00086318 224</p> <p>24</p> <p>25 Schodel-9 9/28/01 E-mail with attachment, MRK-KRA00561416 - 561421 230</p>
<p style="text-align: right;">Page 3</p> <p>1 APPEARANCES (cont'd.) :</p> <p>2</p> <p>3 On behalf of the Defendant:</p> <p>4 VENABLE LLP BY: DINO S. SANGIAMO, ESQUIRE</p> <p>5 and DANIEL A. LOVELAND, JR., ESQUIRE</p> <p>6 750 E. Pratt Street Suite 900</p> <p>7 Baltimore, MD 21202 410.244.7400</p> <p>8 dssangiamo@venable.com daloveland@venable.com</p> <p>9</p> <p>10</p> <p>11 MORGAN LEWIS & BOCKIUS BY: THOMAS J. SULLIVAN, ESQUIRE 1700 Market Street</p> <p>12 Philadelphia, PA 19103 215.963.5146</p> <p>13 thomas.sullivan@morganlewis.com</p> <p>14</p> <p>15 ALSO PRESENT :</p> <p>16</p> <p>17 STEPHEN KRAHLING</p> <p>18</p> <p>19 TIMOTHY K. HOWARD, ESQUIRE Merck in-house counsel</p> <p>20</p> <p>21 - - -</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 5</p> <p>1 E X H I B I T S (Cont'd.)</p> <p>2 Schodel-10 E-mail chain, MRK-KRA00561361 - 561365-00017 261</p> <p>3</p> <p>4 Schodel-11 10/19/01 Letter, MRK-KRA01469018 - 1469020 292</p> <p>5</p> <p>6 Schodel-12 4/25/02 E-mail with attachment, MRK-KRA00544512 - 544538, 544540 - 544543 304</p> <p>7</p> <p>8 Schodel-13 5/7/02 E-mail with attachment, MRK-KRA00544296 - 544324 305</p> <p>9</p> <p>10 Schodel-14 E-mail chain with attachments, MRK-KRA00561199 - 561209 331</p> <p>11</p> <p>12 Schodel-15 E-mail chain, MRK-KRA00791315 - 791319 340</p> <p>13</p> <p>14 Schodel-16 Excerpted document of Clinical Study Report, MRK-KRA00001270 - 1466 357</p> <p>15</p> <p>16 Schodel-17 10/21/03 Memo, MRK-KRA01638866 - 1639147 359</p> <p>17</p> <p>18 Schodel-18 Supplemental Biologics License Application, MRK-KRA00000032 - 139 366</p> <p>19</p> <p>20 Schodel-19 Article draft, MRK-KRA00032482 - 32519 371</p> <p>21</p> <p>22 Schodel-20 10/28/11 E-mail with attachment, MRK-KRA00046402 - 46441 375</p> <p>23</p> <p>24 Schodel-21 E-mail chain, MRK-KRA01481843 - 1481846 & 566614 - 566623 378</p> <p>25</p> <p>26 Schodel-22 2/25/03 E-mail, MRK-KRA00566606 406</p>

Page 6	<p>1 DEPOSITION SUPPORT INDEX</p> <p>2 DIRECTION TO WITNESS NOT TO ANSWER</p> <p>3 Page Line</p> <p>4 21 24</p> <p>5 22 24</p> <p>6</p> <p>7</p> <p>8 REQUEST FOR PRODUCTION OF DOCUMENTS</p> <p>9 Page Line</p> <p>10 (None)</p> <p>11</p> <p>12</p> <p>13</p> <p>14 STIPULATIONS</p> <p>15 Page Line</p> <p>16 (None)</p> <p>17</p> <p>18</p> <p>19</p> <p>20 QUESTIONS MARKED</p> <p>21 Page Line</p> <p>22 (None)</p> <p>23</p> <p>24</p> <p>25</p>	Page 8	<p>1</p> <p>2 MR. MACORETTA: John Macoretta</p> <p>3 from Spector Roseman for private</p> <p>4 plaintiffs as well.</p> <p>5 MR. KRAHLING: Steve Krahlung,</p> <p>6 Relator for the United States of</p> <p>7 America.</p> <p>8 MR. HOWARD: Tim Howard for</p> <p>9 Merck.</p> <p>10 MR. SULLIVAN: Tom Sullivan from</p> <p>11 Morgan Lewis for Merck.</p> <p>12 MR. LOVELAND: Daniel Loveland</p> <p>13 from Venable for Merck and Dr. Schodel.</p> <p>14 MR. SANGIAMO: Dino Sangiamo</p> <p>15 from Venable for Merck and Dr. Schodel.</p> <p>16 VIDEOGRAPHER: Counsel on the</p> <p>17 phone.</p> <p>18 MR. BEGLEITER: Bob Begleiter,</p> <p>19 plaintiffs.</p> <p>20 VIDEOGRAPHER: The court</p> <p>21 reporter is Linda Rossi of Veritext.</p> <p>22 Will the court reporter, please, swear</p> <p>23 in the witness?</p> <p>24 - - -</p> <p>25</p>
Page 7	<p>1</p> <p>2 - - -</p> <p>3 VIDEOGRAPHER: We're now on the</p> <p>4 record. My name is Russ Strain</p> <p>5 representing Veritext Legal Solutions.</p> <p>6 The date today is December 22,</p> <p>7 2016. The time is approximately</p> <p>8 9:05 a.m. This deposition is being</p> <p>9 held at Spector Roseman, 1818 Market</p> <p>10 Street, Philadelphia, PA. The caption</p> <p>11 of this case is In Re: Merck Mumps</p> <p>12 Vaccine Antitrust Litigation, filed in</p> <p>13 the US District Court for the Eastern</p> <p>14 District of Pennsylvania, Case Number</p> <p>15 2:12-cv-03555. The name of the</p> <p>16 witness is Dr. Florian Schodel, MD.</p> <p>17 If counsel at this time will,</p> <p>18 please, introduce themselves for the</p> <p>19 record?</p> <p>20 MR. KELLER: Sure. Jeffrey</p> <p>21 Keller from Keller Grover on behalf of</p> <p>22 Relators.</p> <p>23 MS. ZINSER: Diana Zinser,</p> <p>24 Spector Roseman Kodroff & Willis for</p> <p>25 plaintiffs.</p>	Page 9	<p>1 FLORIAN SCHODEL, MD, after</p> <p>2 having been duly sworn, was examined</p> <p>3 and testified as follows:</p> <p>4 VIDEOGRAPHER: Testimony can now</p> <p>5 proceed.</p> <p>6 - - -</p> <p>7 EXAMINATION</p> <p>8 - - -</p> <p>9 BY MR. KELLER:</p> <p>10 Q. Dr. Schodel, can you state your</p> <p>11 name for the record?</p> <p>12 A. My name is Florian Schodel.</p> <p>13 Q. Have you ever been known by any</p> <p>14 other name?</p> <p>15 A. No.</p> <p>16 Q. Can you tell me your business</p> <p>17 address?</p> <p>18 A. 1623 Pine Street in Philadelphia.</p> <p>19 Q. Have you ever had your deposition</p> <p>20 taken before?</p> <p>21 A. Not in a US court.</p> <p>22 Q. When you had your deposition</p> <p>23 taken outside the US, when was that?</p> <p>24 A. I don't remember. A long time</p> <p>25 ago.</p>

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. I asked that. We'll go over

3 some of the --

4 A. More than 20 years.

5 Q. Okay. We'll go over some of

6 the -- was that for one of your employers or

7 was that a personal matter?

8 A. No, personal matters.

9 Q. Let me go over some of the

10 ground rules to remind you. I'm sure your

11 counsel has sort of walked you through this,

12 but it always helps to kind of go over it

13 before the deposition so it's fresh in your

14 mind.

15 You've -- your testimony today

16 is under oath under the penalty of perjury.

17 At the end of this deposition the court

18 reporter is going to do a great job of writing

19 down everything that you say, that I say and

20 anybody else in the room says. You'll have a

21 chance to review that and make any corrections

22 that you think are appropriate, but I will

23 remind you any changes you make to the

24 transcript we'll be able to comment at trial.

25 Okay?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 A. Okay.

3 Q. Since the court reporter, though

4 she's amazing, can really -- only really

5 capture words, though, she can't say -- if you

6 get up and ran out of the room, she'll write

7 down witness ran out of the room. Try to

8 answer the questions with words, you know,

9 instead of saying uh-huhs and uh-uhs, yes or

10 no would be -- we'll have a much cleaner

11 record if you could do that. Is that fair?

12 A. No problem.

13 Q. Great. I'm going to be asking

14 you questions and you're going to be answering

15 the questions. If you don't understand my

16 question, please let me know; otherwise, we're

17 all going to assume that you understood the

18 question. Is that fair?

19 A. I will not answer a question I

20 can't understand so obviously I will ask you.

21 Q. Perfect. As long as we have the

22 same understanding.

23 We don't want you to guess or

24 estimate unless specifically requested. We

25 want to know what your best understanding of

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2 things so if you don't have a good

3 understanding or if you can't answer the

4 question except by guessing or estimating,

5 please let us know. Is that fair?

6 A. That's fair.

7 Q. As you can tell, the court

8 reporter, again, takes down everything that we

9 say and it's helpful, though I don't think

10 we'll have a problem, is to not talk over each

11 other. Allow me to finish asking the

12 question, though you're already probably going

13 to know what the rest of my question is when I

14 start it, I may pause in the middle as I try

15 to formulate a question, just give me the

16 opportunity to finish the question before you

17 answer. And I'll try to do the same thing

18 instead of asking you the next question before

19 you answer, fully answer, just so we get a

20 nice clean record at the end of the day.

21 Because when the record comes out, it's going

22 to have a question and an answer, and if we

23 talk over each other, the question gets broken

24 up, because she just writes down whatever

25 people are saying when they're saying it.

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2 Dr. Schodel, do you have a

3 personal lawyer?

4 A. For this particular case?

5 Q. Generally, overall.

6 A. Not in the United States.

7 Q. Do you have an attorney for your

8 consulting firm?

9 A. For my firm?

10 Q. Yes.

11 A. No.

12 Q. Who is representing you today?

13 A. They already stated it. The

14 firm Venable.

15 Q. Is Morgan Lewis representing you

16 today?

17 MR. SANGIAMO: That's

18 Mr. Sullivan's firm as well.

19 THE WITNESS: Are they?

20 MR. SANGIAMO: Yes.

21 THE WITNESS: They are.

22 BY MR. KELLER:

23 Q. Did you sign a retainer

24 agreement with them?

25 A. No, I did not.

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2 Q. Are you paying them any fees?

3 A. No, I do not.

4 Q. Have they ever represented you

5 in the past?

6 A. No, they have not.

7 Q. So they only represent you for

8 the purposes of this lawsuit and your deposition

9 today?

10 A. That's correct.

11 Q. Yes?

12 A. Yes.

13 Q. When did you first speak to your

14 counsel for the purposes of this deposition?

15 A. For the purposes of this

16 deposition we spoke in the beginning of this

17 week.

18 Q. Were they retained at the

19 beginning of this week?

20 A. No. A little earlier.

21 Q. Do you know when earlier?

22 A. No.

23 Q. Was it within the past month?

24 A. Yes, probably.

25 Q. How many times have you spoken

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2 to your counsel for the purposes of this

3 deposition?

4 A. Well, directly for the deposition,

5 we've only spoken this week. We have a

6 general discussion earlier.

7 MR. SANGIAMO: Doctor, it's

8 important that you not disclose the

9 content of those prior discussions.

10 So your answer is okay but wait for

11 Mr. Keller's next question.

12 BY MR. KELLER:

13 Q. And you said you had a general

14 discussion. I'm not going to ask you what you

15 discussed, I just want to know when you

16 discussed -- this general discussion you had

17 prior to this week, do you recall when that

18 was?

19 A. I don't recall exactly. I

20 could look it up in my calendar, I had a lot

21 of discussions. I think my first knowledge

22 of the case was triggered by --

23 MR. SANGIAMO: I'm sorry, go

24 head.

25 THE WITNESS: -- somebody called

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2 me and then I got in touch with Merck

3 which was maybe half a year ago, but I

4 don't really remember.

5 BY MR. KELLER:

6 Q. And when you -- somebody from

7 the plaintiff's side of this lawsuit contacted

8 you. Correct?

9 A. Contacted me. And they

10 contacted me in a way that met -- that I

11 thought it was a Merck lawyer because he did

12 not state in the beginning of the phone call

13 who he was representing and started asking me

14 questions. And started asking whether I

15 would be willing to appear as a witness in

16 this case that I didn't know anything about.

17 And it sounded very strange to me. So

18 finally, I asked whether he was representing

19 Merck. He told me that he was not. And by

20 that time I told him that I would talk to

21 Merck and not continue this conversation.

22 Q. Do you recall -- so you called

23 somebody at Merck. Did you call -- who did

24 you call at Merck?

25 A. To tell you the truth, I don't

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2 remember anymore. I don't -- I could

3 probably try to -- I don't remember anymore.

4 But I tried to find somebody at Merck who was

5 responsible for, and then I eventually got to

6 the people who were dealing with this.

7 Q. Did you speak to the legal

8 department at Merck?

9 A. They eventually contacted me

10 back, but they were not my first contact

11 because I wouldn't have known whom to call

12 there.

13 Q. The person who you spoke to at

14 Merck who wasn't one of Merck's lawyers, do

15 you recall what you discussed with them?

16 A. No, I didn't actually discuss

17 anything other than I was contacted by a law

18 firm in regards to a court case that Merck

19 seemed to be involved in and that I wanted

20 Merck to get in touch with me and figure out

21 what needed to be done.

22 Q. Did somebody from the legal

23 department at Merck reach out to you?

24 A. Yes.

25 Q. Do you recall who that person

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 2 was?
 3 A. Tia Clarke.
 4 Q. Can you spell the last name?
 5 A. No. But I can try.
 6 C-L-A-R-K-E maybe. Could be K without an E.
 7 Q. Fair enough. If you identify
 8 people's names, just for the court reporter's
 9 sake, if you -- especially if they have a
 10 spelling that is difficult, it may be helpful
 11 just to spell it as you go. You're going to
 12 have to do it eventually. She's going to ask
 13 you anyway.
 14 A. In that case I simply don't
 15 know. It's probably C-L-A-R-K-E.
 16 Q. Close enough. Just so that we
 17 have -- even if it's phonetic, it's helpful to
 18 have the names.
 19 And then you said that you -- do
 20 you recall how long you spoke to Ms. Clarke?
 21 A. No, I think that was just an
 22 exchange of e-mails.
 23 MR. SANGIAMO: Dr. Schodel, just
 24 make sure you just answer his
 25 question. His question was do you

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 2 know how long you spoke to --
 3 THE WITNESS: I'm not even sure
 4 I spoke to her at all.
 5 BY MR. KELLER:
 6 Q. Do you recall how long -- did
 7 you speak to anybody in the legal department
 8 at Merck?
 9 A. No.
 10 Q. Did Merck refer you to one of
 11 your lawyers that your -- that are
 12 representing you here today?
 13 A. Yes, eventually.
 14 Q. Then you said that you spoke to
 15 somebody -- other than this week, have you
 16 spoken to anybody else at Merck regarding this
 17 lawsuit?
 18 A. No.
 19 Q. Have you spoken to anybody else
 20 other than your lawyers regarding this lawsuit?
 21 A. Yeah, my wife. I told her that
 22 I had to spend the last days before Christmas
 23 giving a deposition.
 24 Q. Did you discuss with her any of
 25 the details?

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 2 A. Bloody detail. No, of course
 3 not.
 4 Q. Fair enough. And then you said
 5 this week you spoke to your lawyers about
 6 preparation for this deposition. Correct?
 7 A. Yes.
 8 Q. And when this week did you speak
 9 to them?
 10 A. Monday.
 11 Q. Monday.
 12 A. Was it Monday? Yeah.
 13 Q. Did you meet them in person or
 14 on the phone?
 15 A. Yes. Or was it Tuesday? I
 16 don't know. I think -- I mean, I have a
 17 lot -- had a lot of stuff on my plate this
 18 week. It may have been another day of the
 19 week. Tuesday.
 20 Q. Your best recollection. I'm not
 21 going to hold you to Monday or Tuesday. So
 22 either Monday or Tuesday you met with them in
 23 person. Do you recall how long you met with
 24 them?
 25 A. Most of the day.

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 2 Q. Most of the day. Did they show
 3 you documents?
 4 A. Yes.
 5 Q. Do you recall how many documents?
 6 A. No. Many.
 7 Q. Many. Is many more than 10?
 8 A. Yes.
 9 Q. Is it many more than 100?
 10 A. No.
 11 Q. More than 20?
 12 A. Probably.
 13 Q. Less than 50?
 14 A. I don't know.
 15 Q. And you reviewed those documents?
 16 A. Yes.
 17 Q. And did any of those documents
 18 help refresh your memory about what was in
 19 those documents?
 20 A. Yes.
 21 Q. Do you recall which of those
 22 documents refreshed your memory as to what was
 23 in those documents?
 24 MR. SANGIAMO: I'm going to
 25 interpose an objection. I'm going to

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 2 instruct Dr. Schodel not to answer
 3 that question.
 4 BY MR. KELLER:
 5 Q. Are you going to follow your
 6 counsel's advice?
 7 A. When you find out as you ask me
 8 about specific documents, which I do remember
 9 and which I don't remember, I couldn't give
 10 you a list off my head which ones I remember
 11 or don't remember. But there were some --
 12 some of them were e-mails that I had written
 13 and I had not remembered them if I hadn't
 14 seen them.
 15 Q. Fair enough. Other than that
 16 full day that you met with your counsel in
 17 preparation for this deposition, have you done
 18 anything else in preparation for this
 19 deposition?
 20 A. No. No.
 21 Q. Did any of the documents that
 22 you looked at, did they surprise you in any
 23 way?
 24 MR. SANGIAMO: Dr. Schodel, I'm
 25 going to instruct you not to answer

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 2 that question. That's invading the
 3 attorney/client privilege and work
 4 product doctrine, legal doctrine. So
 5 I'm instructing you not to answer Mr.
 6 Keller's question.
 7 BY MR. KELLER:
 8 Q. Are you going to follow your
 9 counsel's advice?
 10 A. Yes, I do.
 11 Q. Was there anybody else present
 12 at that meeting either Monday or Tuesday that
 13 weren't lawyers?
 14 A. One more lawyer who is not here
 15 right now.
 16 Q. So they were all lawyers?
 17 A. Yes.
 18 Q. There was nobody from Merck
 19 present at that meeting?
 20 A. No.
 21 MR. KELLER: Do we have Dr.
 22 Schodel's CV? I'm going to mark as
 23 Exhibit 1 a CV of Dr. Schodel that was
 24 produced to us this morning.
 25 - - -

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 2 (Exhibit Schodel-1, Curriculum
 3 Vitae, was marked for identification.)
 4 - - -
 5 BY MR. KELLER:
 6 Q. Exhibit 1 is a document entitled
 7 "CURRICULUM VITAE" which was produced this
 8 morning by your counsel, Dr. Schodel. Is this
 9 your CV?
 10 A. Yes, it is.
 11 Q. Is it current?
 12 A. Yes, it is.
 13 Q. Any reason to believe that the
 14 information here is not accurate?
 15 A. No.
 16 Q. I just want to go over a couple
 17 of things about your educational background.
 18 Can you just give me a quick summary of what
 19 the degrees you have?
 20 A. Yeah, I have a degree in
 21 medicine which is an earned doctorate. So I
 22 wrote a thesis in immunology. I have also an
 23 earned doctorate in microbiology which is a
 24 second doctorate in medical microbiology for
 25 which I wrote another thesis and I have

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 2 the -- it doesn't exist here, it's a
 3 habilitation which is a right to become a
 4 professor and teach.
 5 Q. Can you describe for me what
 6 your understanding of an immunologist is?
 7 A. An immunologist is somebody who
 8 analyzes immune responses in living organisms.
 9 Q. That's what you're trained in?
 10 A. That's one of the things I'm
 11 trained in, yes.
 12 Q. Do you consider yourself an
 13 immunologist?
 14 A. No.
 15 Q. No?
 16 A. No, I consider myself a physician.
 17 Q. Have you ever used your
 18 immunology background as part of any of your
 19 job duties?
 20 A. Yes, of course.
 21 Q. Have you used your immunology
 22 background as part of your job duties at
 23 Merck?
 24 A. Yes.
 25 MR. KELLER: Let me mark as

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 2 Exhibit 2 --
 3 - - -
 4 (Exhibit Schodel-2, LinkedIn
 5 profile, was marked for identification.)
 6 - - -
 7 BY MR. KELLER:
 8 Q. Exhibit 2 is a document that we
 9 pulled down off of LinkedIn -- I'm sorry, that
 10 we pulled in off of LinkedIn, which has a
 11 summary of some of your educational and work
 12 background. Is the information on this
 13 document correct?
 14 A. I have to read it first.
 15 Yes, it seems to be correct. I
 16 mean, I'm just referring to the summary. All
 17 the other stuff, yeah.
 18 Q. Sure. If there's something in
 19 here as we -- if we go through this that you
 20 say that -- you see that's incorrect, feel
 21 free to let me know that.
 22 In the first sentence it says
 23 that you have 20 years of large pharmaceutical
 24 biotech industry and academic experience of
 25 leading teams in the development of vaccines

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 2 and biologics. Is that correct?
 3 A. Yes, only that by now it's
 4 probably longer.
 5 Q. How much longer is that?
 6 A. It's about 30 years now.
 7 Q. 30 years, okay.
 8 Your company that you founded,
 9 what's the name of that company?
 10 A. Philimmune.
 11 Q. What kind of consulting do you
 12 do at your company?
 13 A. I provide advice on developing
 14 biologics or vaccines primarily on the
 15 clinical side, what kind of clinical trials
 16 should be run to meet criteria for licensure
 17 and how something works. I provide some
 18 advice as to strategy on what compounds based
 19 on data may be worth developing and what the
 20 likely regulatory pathway would be for getting
 21 them licensed in different jurisdictions.
 22 Q. Is one of those jurisdictions
 23 the United States?
 24 A. Yes.
 25 Q. So you have a -- you consider

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 2 yourself to have a good understanding of the
 3 regulatory environment in the United States
 4 for getting a vaccine license?
 5 A. Yes.
 6 Q. And that's one of the services
 7 you provide to your clients?
 8 A. Yes.
 9 Q. And that's part of your 30 years
 10 of experience?
 11 A. Yeah.
 12 Q. When you say "clinical trials,"
 13 can you give me your understanding of what
 14 clinical trials you're referring to?
 15 A. Well, any clinical trial which
 16 means any trial that puts a compound into
 17 humans and tests what happens, whether that's
 18 safety in Phase I, whether it's safety and
 19 immunogenicity or whether it is other
 20 endpoints for the purpose of licensure.
 21 Q. When you say "endpoints," what
 22 do you mean by "endpoints"?
 23 A. Endpoints are in the end what
 24 you measure to determine whether something is
 25 safe or efficacious.

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 2 Q. When you say "efficacious," what
 3 do you mean by "efficacious"?
 4 A. Efficacious means that it
 5 prevents a disease.
 6 Q. I apologize to have you define a
 7 lot of these terms, they seem very rudimentary,
 8 I do that to make sure that we're all on the
 9 same page.
 10 A. Perfectly fine.
 11 Q. Have you ever done any work with
 12 your consulting company for Merck?
 13 A. A single time I have, yes. A
 14 single time I have.
 15 Q. So they're a client?
 16 A. They're not a current client.
 17 Q. Do you hope to do more work for
 18 them in the future?
 19 A. I can't speculate.
 20 Q. Would you like to do more work
 21 for them in the future?
 22 A. I would like to do work for
 23 anybody who needs me.
 24 Q. Including Merck. Correct?
 25 A. Including Merck.

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2 Q. Let me go back to your Exhibit 2

3 which is the -- your LinkedIn page. In the

4 second paragraph to the bottom it says,

5 "Florian joined MRL in 1996...." Do you see

6 that?

7 A. Yes.

8 Q. And MRL, what does that refer

9 to?

10 A. Merck Research Laboratories.

11 Q. ...as Director of Clinical

12 Vaccine Research leading EU vaccine clinical

13 trials in the clinical development of

14 rotavirus, measles, mumps and rubella

15 vaccines. Do you see that?

16 A. Yes.

17 Q. What does EU stand for?

18 A. The European Union.

19 Q. Do you recall what clinical

20 trials you worked on during this time frame

21 that you were working for Merck in Europe with

22 respect to the mumps vaccine?

23 A. Those are several questions in

24 one. With respect to the mumps vaccine, I

25 don't remember any trial in the EU, although

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2 there might have been an EU arm so I don't

3 really remember details of the trials. I

4 know that there was a -- that the end expiry

5 trial was being performed, but whether it was

6 performed in the EU, I don't remember.

7 Q. And "the end expiry trial," can

8 you describe what you mean by that?

9 A. That was a trial to determine

10 whether a lower dose of mumps at the end of

11 its shelf life would still yield the same

12 immune response as a higher titer obviously.

13 Q. So is the purpose to see whether

14 or not -- if Merck sold the vaccine at a lower

15 dose, whether or not that would protect kids

16 in the same way that a higher dose would?

17 A. No, that's a --

18 MR. SANGIAMO: Object to the

19 form. You can answer.

20 THE WITNESS: I think that -- so

21 you're sort of leading into something

22 which is not -- the premise is wrong.

23 It's not a matter of whether was Merck

24 selling something that -- at a lower

25 dose. Merck wasn't planning to sell

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2 something at a lower dose. But by

3 that time the labeling philosophy had

4 changed or was about to change, hadn't

5 quite changed yet, both from an FDA

6 perspective and from a company

7 perspective. The old labels

8 originally just stated a number which

9 was found to be efficacious in a

10 clinical trial, whatever that number

11 was. Some of these numbers became

12 compendial, by the way. Then over

13 time the understanding started to be

14 that a vaccine needed to maintain that

15 number that was stated in the label

16 throughout the shelf life. So that

17 was a change. And because that was

18 not the case when mumps was originally

19 licensed 40 years ago, Merck had to

20 make sure that whatever was in the

21 vaccine throughout shelf life

22 maintained its efficacy. So that the

23 label statements would be as of the

24 current understanding which had

25 changed.

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2 So Merck wasn't trying to sell

3 anything different. It was always

4 selling the same thing. It was just

5 providing additional -- actually being

6 quite diligent in providing additional

7 information about the clinical

8 behavior of the vaccine it was

9 selling.

10 BY MR. KELLER:

11 Q. When you say "compendial," can

12 you describe what that means?

13 A. Yes. There are some compendia

14 that define concentrations or potencies of

15 certain things like the pharmacopeia. And in

16 some cases they provide numbers for vaccines.

17 So, for example, in the European Union there

18 is a compendium that states essentially, I

19 don't know the exact text, but that states

20 essentially that a mumps vaccine will have

21 3.7 logs of mumps virus.

22 Q. In that 3. --

23 A. So that becomes a -- rather

24 than something that a company has tested,

25 that becomes a leading requirement for a

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 2 vaccine to have that number in it.
 3 Q. So in the US, do you recall it
 4 being a higher number?
 5 A. I don't recall the US having a
 6 compendial statement at all.
 7 Q. Do you recall that in the US
 8 that the label required that the mumps vaccine
 9 have a certain potency?
 10 A. Yes, but with the caveat what I
 11 just said, understanding of what that meant
 12 had changed over time.
 13 Q. Gotcha. But it did have a
 14 certain potency?
 15 A. Yes, but originally --
 16 MR. SANGIAMO: Dr. Schodel, make
 17 sure you let Mr. Keller finish his
 18 question.
 19 I'm sorry. Could you restate
 20 your question, please, Jeff?
 21 MR. KELLER: Sure. Can you read
 22 it back?
 23 - - -
 24 (The court reporter read the
 25 pertinent part of the record.)

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 2 - - -
 3 BY MR. KELLER:
 4 Q. But you understood that the
 5 label in the United States did have a certain
 6 required potency for the vaccine?
 7 MR. SANGIAMO: Object to the
 8 form.
 9 THE WITNESS: Yes.
 10 BY MR. KELLER:
 11 Q. And the question was whether or
 12 not that potency had to be not just at release
 13 but also at the end expiry of the vaccine.
 14 Correct?
 15 A. That is correct.
 16 Q. When you say "potency," can you
 17 define for me what you mean by "potency"?
 18 A. Potency is -- I mean, it's
 19 defined in the CFR, but potency in this
 20 particular case means a certain quantity of
 21 virus that leads to a biologic effect in an
 22 in vitro assay. In that case it's a plaque
 23 neutralizing reduction assay. So it -- a
 24 plaque -- it's a plaque assay, neutralizing
 25 reduction is the antibody assay. It's a

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 2 plaque -- it's a plaque assay, so many units
 3 in there that when you put them in cell
 4 culture, they produce holes in the cell
 5 culture which are counted as plaques.
 6 Q. So when you say, "a plaque
 7 assay," are there different plaque assays?
 8 A. Yeah. There are all kinds of
 9 different assays to measure potency. They
 10 could be fluorescent assays. They could
 11 be -- it's just -- they're just measures to
 12 quantitate the amount of a live product.
 13 Q. So the plaque assay, is that a
 14 plaque reduction neutralization assay?
 15 A. No, that's the antibody assay.
 16 MR. SANGIAMO: Object to form.
 17 You can answer.
 18 BY MR. KELLER:
 19 Q. So the plaque assay there is
 20 used for potency, is that -- it's just
 21 identifying how many viruses are in each dose.
 22 Correct?
 23 A. How many live viruses are in
 24 each dose. And it's not -- the assay is not
 25 as important as the -- I mean any assay could

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 2 be validated to show that it does the same
 3 thing as long -- and as long as it's shown to
 4 do the same thing, it would meet those
 5 criteria. But it's, of course, defined in
 6 defining documents. I don't remember exactly
 7 what Merck did there.
 8 Q. So there's protocols that set
 9 for how these assays are run. Correct?
 10 A. Yes.
 11 Q. And those assays are validated
 12 some --
 13 A. Yes.
 14 Q. -- to a certain extent.
 15 Correct?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 BY MR. KELLER:
 19 Q. Let me strike the question.
 20 These assays, these potency
 21 assays are validated. Correct?
 22 A. Yes.
 23 Q. Who does the validation?
 24 A. That is not my responsibility
 25 but I think it's the manufacturing department

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 2 that validates the release assay.
 3 Q. You said that the label
 4 philosophy had changed at a certain point
 5 during your tenure at Merck regarding the end
 6 expiry versus whether or not, if I understand
 7 you correctly, the release potency would be
 8 the same or different from the end expiry
 9 potency. Correct?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 BY MR. KELLER:
 13 Q. Do you understand my question?
 14 A. The first part yes. The second
 15 part no. So the first part has a change.
 16 Yes, it has changed. It has nothing to do
 17 with Merck. It has changed overall for the
 18 whole industry. The second part wasn't clear
 19 to me.
 20 Q. Sure. When you say it's changed
 21 for the whole industry, can you describe what
 22 you mean by that?
 23 A. Well, that in general the idea
 24 of how -- what the guarantee in the label had
 25 evolved and the science had evolved. I think

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 2 most labels were written 40, 50 years ago
 3 with a description of the product that did
 4 not include either maximum release or minimum
 5 release potencies but just simply a number.
 6 Q. And then that changed from a
 7 regulatory standpoint?
 8 A. It changed both from a
 9 regulatory and from a company standpoint in
 10 the sense that it was clarified what these
 11 things mean.
 12 Q. So there is a clarification
 13 between -- you say clarified, clarified by
 14 who?
 15 A. Ultimately by the agencies.
 16 Q. So in the case of the US, the
 17 FDA?
 18 A. Yes.
 19 Q. Were you involved at all in any
 20 of the discussions with the FDA regarding this
 21 change in requiring a maximum and minimum
 22 potencies?
 23 A. Not explicitly but implicitly,
 24 yes.
 25 Q. When you say "implicitly," can

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 2 you describe what you mean by that?
 3 A. Well, because as that became
 4 the requirement for new products, every new
 5 product that would be licensed had to meet
 6 these kinds of expectations and, therefore,
 7 there was always a discussion as to what the
 8 data were to support these numbers.
 9 Q. So this change that occurred, do
 10 you recall when that change was?
 11 A. Not specifically. But I think
 12 it evolved in the time period between 1990
 13 and 2000 roughly, and then the years thereafter.
 14 Q. And so this change in the
 15 requirement, do you recall Merck having any
 16 discussions that you became aware of with
 17 respect to this requirement of having an end
 18 expiry potency?
 19 A. Yes.
 20 Q. Were you involved in those
 21 discussions directly with the FDA?
 22 A. No, not -- certainly not
 23 initially. As specific protocols or filings
 24 were discussed, I may have been part of some
 25 of those discussions.

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 2 Q. Were you involved in the end
 3 expiry study that we talked about earlier?
 4 A. Yes, on and off.
 5 Q. Did you help develop original
 6 protocols?
 7 A. No.
 8 Q. Do you know who developed
 9 original protocols?
 10 A. I know it on the biometric side
 11 but not the clinical side.
 12 Q. Who about on the biometric side?
 13 A. Tim Schofield. At least that
 14 was my recollection.
 15 Q. Do you recall -- what role did
 16 you play at all in this end expiry study?
 17 A. Well, I was supervisor of the
 18 physicians who were responsible for mumps
 19 where I was directly responsible for a short
 20 time for anything that had to do with MMR or
 21 MMR/V. But that changed various times. So
 22 at times I had physicians report to me who
 23 were responsible for MMR or MMR/V.
 24 Q. And MMR/V, that's ProQuad.
 25 Correct?

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 2 A. ProQuad, yes.
 3 Q. Let me just sort of frame the
 4 time frame on this. You said at some point
 5 your duties changed. You were a supervisor of
 6 folks, doctors that were responsible for
 7 MMR II. Correct?
 8 MR. SANGIAMO: Mr. Keller, are
 9 you okay with Dr. Schodel looking at
 10 his CV --
 11 BY MR. KELLER:
 12 Q. Absolutely. Whatever helps
 13 refresh your memory, that's fine.
 14 A. That wouldn't give you the
 15 information and I have to say that I don't
 16 remember the exact timing anymore because
 17 that was -- in the time frame between the end
 18 of '96 when I started and roughly '98, I was
 19 on and off. I was assuming more
 20 responsibilities. MMR was certainly not the
 21 focus of my work. It was much more rotavirus
 22 and a number of things and clinical trials in
 23 Europe. But over time I got more of that
 24 responsibility as well.
 25 When the formal reporting lines

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 2 changed, I really don't remember. And then I
 3 wasn't at Merck for about two years. And
 4 when I came back -- I still worked for Merck
 5 as a contractor or consultant but only on one
 6 approach, it had nothing to do with MMR. In
 7 that time period between '98 and 2000 I
 8 didn't work for Merck on the MMR.
 9 Then when I came back, MMR was
 10 initially not under me. I think it was still
 11 under Jerry Sadoff. And it may have been
 12 Scott Tyler or Mike Severino who were the
 13 responsible physicians not reporting to me.
 14 And then at some point after 2000, maybe 2002
 15 or so, 2001, 2002, I became formally
 16 responsible for these vaccines.
 17 Q. So according to -- I'm looking
 18 at your LinkedIn summary of your work
 19 experience. It has you starting at Merck
 20 Europe in 1996 through November of 1998. Were
 21 you working in Europe or were you working in
 22 the United States?
 23 A. Half and half.
 24 Q. And then in November 2000 -- and
 25 you left for a company outside of Merck and

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 2 then came back in November 2002 -- 2000,
 3 sorry, and where you held executive director
 4 of vaccine integration through March of 2002.
 5 Do you see that?
 6 A. Yes.
 7 Q. What is vaccine integration?
 8 A. Vaccine integration was a
 9 department at the time which was created in
 10 anticipation of a number of vaccine filings,
 11 quite a few, which made sure that the
 12 different departments of Merck collaborated
 13 in putting together the right data for the
 14 filings.
 15 Q. Is that more focused on new
 16 vaccines versus existing vaccines?
 17 A. No, it was responsible for
 18 certain aspects of both. For example, we
 19 developed a way how to write the CTD in
 20 electronic form. So it had various -- it had
 21 a direct clinical team which was very small.
 22 And that was more focused on new things, but
 23 then it had a larger role across different
 24 departments.
 25 Q. Let me just sort of back up so I

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 2 can understand what your actual duties were at
 3 Merck and then we can sort of walk through.
 4 When you started in 1996 through
 5 that 1998 time frame as a director of clinical
 6 vaccine research, what were your duties? We
 7 can limit it really -- let me ask that
 8 generally. What were your duties generally?
 9 A. In general, I had a small group
 10 that was responsible for the operational
 11 aspects of clinical trials in Europe. So
 12 working with the CROs, working with the
 13 investigators, making sure that we had the
 14 sites ready and so on. So more operational
 15 work.
 16 I was also the liaison to the
 17 joint venture with Sanofi Pasteur in Europe
 18 and sat on the clinical development team for
 19 Hexavac which was a vaccine that we
 20 co-developed with Sanofi at the time. That
 21 was a major part of my responsibilities, and
 22 I represented Merck on that team for clinical
 23 issues.
 24 Then in the US, as I mentioned
 25 earlier, I was primarily responsible as a

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2 monitor for the new rotavirus vaccine, so I

3 developed a clinical development plan for

4 RotaTeq. And those were really the main

5 responsibilities. That's what I spent most

6 of my time on, between --

7 Q. So your role with respect to the

8 MMR vaccine was very limited during this time

9 frame?

10 A. At that time, my role was

11 limited, yes.

12 Q. The rotavirus vaccine, did you

13 conduct clinical studies with that vaccine?

14 A. Yes. Yes.

15 Q. What were the studies -- what

16 were the assays that were run in that, with

17 that particular vaccine?

18 A. Well, I mean, there were a

19 number of ELISAs run to measure antibody

20 titers and functional assays to measure

21 neutralization of viruses as well.

22 Q. When you say a functional assay,

23 could you describe what you mean by a

24 functional assay?

25 A. A functional assay would be an

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2 assay that is a neutralization assay that

3 basically mixes the virus with the antibodies

4 in a test tube and see whether the virus

5 activity on a cell log gets reduced.

6 Q. So it either kills it or stops

7 it from growing. Is that fair?

8 A. Yes. It could. Yes. Or stops

9 it from entering a cell.

10 Q. Gotcha. So in this, the

11 neutralizing assays that you did for the

12 rotavirus, was that a plaque reduction

13 neutralization assay?

14 MR. SANGIAMO: Object to the

15 form.

16 THE WITNESS: First of all, I

17 didn't do these assays.

18 BY MR. KELLER:

19 Q. Fair enough.

20 A. So I was responsible for the

21 clinical part. And secondly --

22 Q. Let me back up.

23 A. Secondly, there were different

24 formats tried. I don't even remember anymore

25 exactly which one which was in the end. I

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2 think they were microneuts, but I don't --

3 Q. Okay. Fair enough. What is the

4 difference -- is the ELISA a functional assay?

5 A. No. It's a binding assay.

6 Q. Binding assay. What do you mean

7 by "a binding assay"?

8 A. Measures whether an antibody is

9 bound to a substrate which could be a cell,

10 could be an antigen that is fixed in the

11 plate.

12 Q. And so what is the -- an ELISA

13 assay, how is that reported in terms of

14 reporting?

15 A. The ELISA assay reports, it has

16 a substance added to the test tube which by

17 virtue of an enzyme is converted from one

18 form to the other and then changes color.

19 And that color change is measured. So if a

20 lot of antibody is in there, the antibody is

21 tagged with an enzyme. A lot of enzyme in

22 the tube and that enzyme causes a color

23 change and the color change is measured.

24 Q. So your -- it's an optical test

25 to identify a number of optical units. Is

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2 that a fair way to say it?

3 A. Yes, although most tests are

4 optic because you have to look at them. So

5 when you count them, that's an optical test,

6 too, in a way.

7 Q. Gotcha.

8 A. But this is one where you

9 measure color change specifically. So the

10 change of light absorption.

11 Q. How is that reported?

12 A. Many different --

13 MR. SANGIAMO: Jeff -- excuse

14 me. Jeff, you're saying how is that

15 reported?

16 MR. KELLER: Yes.

17 MR. SANGIAMO: Okay.

18 THE WITNESS: It can be reported

19 just as an optic density change at a

20 given dilution. That would be the

21 simplest form. It can be reported as

22 a titer, a titer being defined by

23 certain criteria.

24 BY MR. KELLER:

25 Q. So when it's done as a titer, do

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2 they usually typically report that as a

3 seroconversion?

4 A. Those are two different

5 concepts. Seroconversion means that a serum

6 that previously was negative or lower by

7 defined measure becomes now higher in content

8 of antibody as measured by an ELISA or any

9 other assay for that matter. So that's not --

10 Q. That's a way to use ELISA --

11 utilize a test is to report --

12 A. The ELISA test would be what

13 you measure. The seroconversion would be

14 what you calculate out of that.

15 Q. How would you determine when

16 you're calculating what you're measuring,

17 whether or not it's a seroconversion or not?

18 A. Well, you compare pre and post.

19 So a seroconversion means that a serum that

20 previously contained no or little antibody

21 contains now some antibody above a certain

22 threshold. Or a serum that contained a

23 quantity of antibody in the first test now

24 contains ten times more antibody. So it

25 contains more by some defined measure as any

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2 which way you define that.

3 Q. So either you can do it by a

4 fold factor or a cutoff. Is that correct?

5 A. That is correct, yes.

6 Q. And when you do it by a

7 cutoff -- did you ever hear the term

8 "serostatus cutoff"?

9 A. Yes.

10 Q. What does that mean?

11 A. It means that a number in that

12 particular assay under standardized

13 conditions determines whether you have a

14 higher likelihood to be negative or positive.

15 In other words, it divides a cohort of people

16 into those that have -- likely have and

17 likely do not have antibodies.

18 Q. How do you determine whether --

19 what that serostatus cutoff is?

20 A. By using negative and positive

21 sera.

22 MR. SANGIAMO: Object to the

23 form. You can answer.

24 BY MR. KELLER:

25 Q. Can you describe that process?

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2 MR. SANGIAMO: Object to the

3 form. You can answer.

4 THE WITNESS: Yeah. You find a

5 collection of sera that by a

6 comparator assay have been -- or by

7 history have been known not to have

8 been exposed by whatever you're

9 measuring. And you run your new assay

10 and you see how it classifies. It's a

11 classification comparison if you want.

12 That's at least one way of doing it.

13 There are other ways that you can use.

14 BY MR. KELLER:

15 Q. So that -- is that called a

16 control?

17 A. No. No, it's not. A control

18 would be something that you run within the

19 assay to determine whether the particular

20 assay run has actually worked the way you

21 predict it to work.

22 Q. And so the way to determine it

23 by a factor, how does that work?

24 MR. SANGIAMO: Object to the

25 form.

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2 THE WITNESS: Well, the factor

3 is -- it depends on how you define it.

4 There's many ways of defining a

5 factor. If you -- we're still talking

6 about a serostatus cutoff factor.

7 Right? Just to clarify the question.

8 What factor are you talking about?

9 BY MR. KELLER:

10 Q. Let me just clarify that. I

11 believe you testified that there's two ways,

12 at least two ways to identify a

13 seroconversion, one is by doing it by a cutoff

14 and the other way was doing it by a

15 factoring --

16 A. Oh, you mean that kind of a

17 factor?

18 Q. Yes.

19 A. Well, the factor again can be

20 determine in different ways. The most

21 commonly used ones are the very classic one

22 which comes out of sero dilutions which

23 basically uses two dilutions as a factor, so

24 that's the famous fourfold rise. That's has

25 been introduced because in dilution

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 2 experiments twofold is something that can
 3 generally reliably be pulled apart. A single
 4 dilution is hard to tell apart and you make
 5 an error, so it's too variable. Twofold is
 6 generally something that you can easily hold
 7 apart. In an era long gone in which most
 8 assays were done by sero dilutions, the
 9 fourfold has become more and more a standard.
 10 Even it's not a perfect standard but it is an
 11 average standard that works reasonably well
 12 for that particular purpose. It's really an
 13 old concept coming out of sero dilutions.
 14 The other I think --
 15 MR. SANGIAMO: I'm sorry,
 16 Doctor. Mr. Keller, what was your
 17 last question?
 18 MR. KELLER: He wasn't done.
 19 Let him finish answering, then you can
 20 go back and --
 21 THE WITNESS: It was about the
 22 different ways of determining a factor
 23 or the different factors. So one was
 24 the fourfold. The other one would be
 25 one in which you determined the

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 2 variability of the assay and
 3 determined a factor that clearly
 4 surpasses the variability of the assay
 5 at a given quantity. And, therefore,
 6 it's actually a better way of
 7 determining a factor in a way because
 8 it tells you, say, for example, your
 9 assay is very -- has a very low
 10 standard deviation and you can easily
 11 determine the twofold difference.
 12 Then a better cutoff would be whether
 13 something is changed by twofold from
 14 the start. You can easily imagine
 15 that it depends on the units and it
 16 depends on the accuracy of the assay.
 17 BY MR. KELLER:
 18 Q. So doing a fourfold analysis is
 19 another way to determine if your cutoff is
 20 correct or not?
 21 MR. KELLER: Why don't you just
 22 read the question back.
 23 Let me strike the question.
 24 I'll say it over.
 25 BY MR. KELLER:

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 2 Q. Is one way to identify if the
 3 cutoff that's used to determine seroconversion
 4 in an ELISA assay to check it against a
 5 fourfold analysis to see whether or not that
 6 cutoff is correct?
 7 MR. SANGIAMO: Object to the
 8 form.
 9 THE WITNESS: No. The two are
 10 different concepts.
 11 BY MR. KELLER:
 12 Q. But they're both -- the two
 13 concepts are different ways of showing the
 14 same thing. Correct?
 15 A. Not exactly.
 16 MR. SANGIAMO: Object to the
 17 form.
 18 BY MR. KELLER:
 19 Q. How is that -- how are they
 20 different?
 21 A. One is an absolute number that
 22 with a high likelihood differentiates a group
 23 into two different states, positive or
 24 negative or having antibodies or not having
 25 antibodies. The other one is simply a

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 2 measure derived from the presumed variability
 3 of an assay saying you can likely
 4 differentiate the two but they can be both
 5 positive, for example. I mean, a fourfold
 6 rise could be something that's already
 7 positive and becomes -- so they're really
 8 different concepts.
 9 Q. When you talk about the absolute
 10 number, that's having a set serostatus cutoff
 11 as a number. Correct?
 12 A. That's right.
 13 Q. When you say a highly -- "a high
 14 likelihood," is there a percentage at which
 15 you would expect that you'd have that
 16 probability of it being the number that would
 17 most closely resemble -- let me strike that.
 18 What do you mean by "a high
 19 likelihood"? Is there a percentage --
 20 A. It depends on the circumstances.
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: It depends on the
 24 circumstances. It could be anything
 25 you predefine. I mean, you can

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 2 define -- you can, for example,
 3 predefine that you want to have a 95
 4 percent likelihood that a serum you
 5 stated within that example is
 6 seropositive rather than seronegative.
 7 You could define and have a 80 percent
 8 likelihood or a 50 percent likelihood.
 9 Whatever you want to define. And the
 10 definitions then translate into what
 11 your cutoff would be.
 12 BY MR. KELLER:
 13 Q. Gotcha.
 14 MR. SANGIAMO: Doctor, it would
 15 be helpful if you just pause before
 16 you start to answer Mr. Keller's
 17 question. Give me a chance to
 18 evaluate whether I need to object or
 19 not.
 20 THE WITNESS: Okay.
 21 BY MR. KELLER:
 22 Q. When you say that -- in those
 23 numbers, the 95, 85 or 50 percent, are those
 24 -- are those typically written in a protocol
 25 or how are those determined? Are they

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 2 determined before you run the -- before you
 3 run the assay or is it something that you
 4 learn from running the assay?
 5 MR. SANGIAMO: Object to the
 6 form.
 7 THE WITNESS: They could be
 8 either. It depends for what purposes
 9 you are defining them. If you have
 10 already pre-established a serostatus
 11 cutoff, for example, out of a
 12 validation experiment and you've used
 13 whatever criteria you've used, you
 14 could now run a prospective control of
 15 that serostatus cutoff with any given
 16 set of samples. With any given set of
 17 samples you would expect it to be a
 18 little different and you could say,
 19 okay, does this serostatus cutoff that
 20 I have predefined in this new
 21 experiment reliably differentiate the
 22 negatives, the likely negatives from
 23 the likely positives.
 24 BY MR. KELLER:
 25 Q. Is there a -- sort of an

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 2 industry standard for doing, you know,
 3 immunogenicity testing with ELISA as to what
 4 percentage you would want to see as a
 5 likelihood of the cutoff being correct?
 6 A. No.
 7 Q. Is there a rule of thumb?
 8 MR. SANGIAMO: Object to the
 9 form.
 10 THE WITNESS: I don't know.
 11 BY MR. KELLER:
 12 Q. If you're using an ELISA assay
 13 that relies upon a serostatus cutoff that's
 14 being used for purposes of determining whether
 15 or not what you're testing will ultimately
 16 protect somebody from getting sick in the
 17 future based on that antigen, is there a
 18 standard that comes to your mind or a
 19 percentage that comes to your mind that you'd
 20 like to see in terms of the accuracy of that
 21 serostatus cutoff?
 22 MR. SANGIAMO: Object to the
 23 form.
 24 THE WITNESS: There are too many
 25 assumptions in your question. And let

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 2 me just deconstruct them one by one.
 3 BY MR. KELLER:
 4 Q. Sure.
 5 A. So the first assumption is that
 6 the assay is directly correlated to
 7 protection. I'm just leaving it there
 8 because you don't know that it in most cases.
 9 The second one is that there is
 10 a given predetermined percentage that should
 11 be one way or the other the way I understood
 12 your assay. And that is it really also
 13 depends on the circumstances.
 14 Q. Let me ask you, if there's no
 15 correlate of -- let me back up. You say a
 16 correlation of protection. What do you mean
 17 by that?
 18 A. A correlation of protection
 19 would be a measure by which you could
 20 predetermine whether somebody is protected or
 21 has a very high likelihood of not acquiring a
 22 disease. It's different from -- leave it at
 23 that.
 24 Q. So if -- you said that's one of
 25 the criteria, whether or not there's a

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 2 correlate of protection and the other was if
 3 there's a predetermined percentage that you're
 4 looking for. How are those two related, if
 5 they're related at all?
 6 A. Well, if you have a very strong
 7 correlate of protection, let's use the case
 8 of hepatitis B for example where 10 million
 9 international units is fairly well defined
 10 and accepted as a correlate, and then a
 11 second premise would be that you know that a
 12 vaccine elicits a very high level of
 13 protection with that correlate, then you want
 14 to make sure that the accuracy at which you
 15 determine it is also pretty high. So it's in
 16 the 90 and above percent range. That is, you
 17 know, it depends on how reliable the assay is
 18 obviously because the correlate can't be very
 19 precise if the assay to measure is not very
 20 precise. And it depends on how well you know
 21 that the correlate actually really
 22 correlates. Now, if there have been
 23 prospective randomized double blinded
 24 efficacy trials in which a correlate has been
 25 clearly and unequivocally established, that's

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 2 sort of that best kind of data to have,
 3 exists in very, very few disease. Where that
 4 exists, you have a very high standard of
 5 expectation on an assay that would mimic that
 6 kind of a correlate.
 7 Q. Gotcha. When you say -- when
 8 you talk about precision, what do you mean by
 9 precision, "precise"?
 10 A. Well, there is a definition
 11 which I'm probably not able to exactly
 12 reproduce.
 13 Q. Your best understanding.
 14 A. It means that the -- and I
 15 don't know the exact biometrically definition
 16 of precision, but it means that the assay can
 17 reproducibly and accurately reflect the
 18 analytical truth.
 19 Q. Of what you're testing?
 20 A. Of what you're testing.
 21 Q. From the standpoint of an ELISA
 22 assay, you would want to have an ELISA assay
 23 that's precise that it's only counting, for
 24 example, in the mumps case, mumps antibodies
 25 versus any other antibodies that may be in

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 2 that blood sample. Correct?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 THE WITNESS: That's true for
 6 any assay, yes.
 7 BY MR. KELLER:
 8 Q. When you say "any assay," would
 9 that be true for a plaque reduction
 10 neutralization assay?
 11 A. In principle, yes.
 12 Q. You said that -- you mentioned
 13 that there's very few correlates of protection
 14 that you're aware of. Can you identify if
 15 there's any correlates of protection in the
 16 mumps, measles, rubella vaccine?
 17 A. Yes, there is one for measles
 18 which is not quite straightforward because it
 19 was run in an assay format that is no longer
 20 run by anybody. And it has been differently
 21 transcribed into different numbers. But it's
 22 the only one that has a very clear,
 23 established, recognized correlate.
 24 Q. So there's no clear established
 25 recognized correlate for mumps or rubella?

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 2 A. No.
 3 Q. You say that when the -- for
 4 measles it's comparable because the assay
 5 format has changed over time. What do you
 6 mean by that?
 7 A. Well, that -- I don't recall
 8 the exact way how this was established
 9 originally, but I remember that it was
 10 established in a series of cases that were
 11 linked to the preexistence of antibodies in
 12 the serum of people who became cases. And
 13 there was a cutoff established which was
 14 originally based on a neutralization assay
 15 and then translated into an ELISA. And there
 16 is debate as to how that translation actually
 17 was done and whether the ELISA number
 18 shouldn't be different from the number that
 19 is yet defined in a lot of literature. So
 20 there's -- some people reported 120 number
 21 and others reported 255. The 255, I think,
 22 is better researched.
 23 Q. So when you say -- when you're
 24 comparing -- is what they did with that
 25 neutralizing assay when they compared it to

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2 the ELISA assay, is that called -- did they

3 correlate those two assays together?

4 A. You could call that a

5 correlation, yes.

6 Q. Is there other ways to compare

7 two assays to see if they get the same result?

8 A. Yes, by what you just mentioned

9 previously, for example, by their power to

10 distinguish different groups, negatives and

11 positives. Do they distinguish the same

12 groups, do they categorize them the same way.

13 Q. When they do that, is that

14 called a correlation analysis?

15 MR. SANGIAMO: Object to the

16 form.

17 BY MR. KELLER:

18 Q. Or some other term?

19 A. I don't know whether -- what

20 specific term is really used for that.

21 Q. When you say that they're

22 comparing the two groups, if the two groups --

23 can you describe that process, how you do

24 that?

25 A. Well, if you have a group, say,

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2 of a given number of positives, a given

3 number of negatives and they measure them in

4 the two assays and you put them in a 4-by-4

5 table in which you see essentially how the

6 different assays classify them, you will see

7 those that are positive in both assays, that

8 are negative in one and positive in the other

9 or negative in both assays. And then you

10 can -- it's more -- I would call that a

11 concordance testing rather than a correlation

12 testing.

13 Q. And those concordance testing,

14 how important is that that the information

15 match up and how important is it to the extent

16 they don't match up?

17 MR. SANGIAMO: Object to the

18 form. You can answer.

19 THE WITNESS: All assays are

20 artificial. They're all a specific

21 creation of measures to approximate,

22 to approximate the true biological

23 nature of what you're measuring. So

24 you're measuring two different assay

25 systems. You would expect them not to

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2 be completely concordant because

3 you're measuring different things. It

4 depends on the circumstances how

5 important it is for your conclusion

6 from that that they are exactly the

7 same or not. It also depends on how

8 variable they both are. For example,

9 if you compare one relative variable

10 or even fragile assay to one that's

11 very well established and very robust,

12 you may find different correlations

13 every time you do the correlation.

14 BY MR. KELLER:

15 Q. Gotcha. So when you're doing

16 this concordance assay, you're looking at the

17 result that are concordant and you're looking

18 at what's also the discordant. Correct?

19 A. That's correct.

20 MR. SANGIAMO: Object to the

21 form.

22 BY MR. KELLER:

23 Q. Is there a standard way to

24 describe those discordant rights as false

25 positives or false negatives? Do those terms

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2 sound familiar to you?

3 MR. SANGIAMO: Object to the

4 form.

5 THE WITNESS: That -- well, that

6 is a way they are sometimes described,

7 but that assumes that you know the

8 truth, which is sometimes neither here

9 nor there. Sometimes they're just

10 simply different and you have to find

11 out why they're different if it's

12 important. But it doesn't necessarily

13 mean that there's a false negative or

14 a false positive.

15 BY MR. KELLER:

16 Q. Is there a --

17 A. But if you take one for the

18 truth and the other one for the experiment,

19 then, yes, you can use those terms.

20 Q. So in the case where you're in

21 the measles context, you are -- the folks in

22 those assays were doing a concordance analysis

23 between a neutralizing assay and an ELISA

24 assay. Is that correct?

25 A. I'm not sure that they ever did

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 2 that. I'm not sure what they ever did. I
 3 just found that in some of the papers that
 4 were written relatively shortly after the
 5 observation, that there was a certain titer
 6 that correlated with a low likelihood of
 7 becoming a measles case, all of a sudden that
 8 switched to ELISA titers and the ELISA titers
 9 may or may not have been really the same
 10 numbers. So I think this is not a formal
 11 concordance testing, at least I'm not aware
 12 of it. It is more an error in transcription.
 13 Q. I see.
 14 A. And then later on actually the
 15 255 was based on a -- to the best knowledge
 16 at the time an effort to correlate the ELISA
 17 as it was then run with the old data in the
 18 literature.
 19 Q. And that correlation, how is
 20 that correlation used for purposes of -- from
 21 a regulatory standpoint?
 22 A. I don't know exactly. Because
 23 just to remind you, the basis of licensure
 24 for these vaccines is generally
 25 noninferiority which is not an absolute

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 cutoff alone. So how was it used for
 3 regulatory purposes, I don't think it was --
 4 - - -
 5 (Interruption.)
 6 - - -
 7 MR. SANGIAMO: Mr. Keller, if
 8 anyone enters the conference, they
 9 ought to say who they are, but I would
 10 also appreciate if people not enter
 11 and then leave. And perhaps if anyone
 12 wants to enter, they can contact
 13 someone here find out when there's a
 14 break and they can enter during a
 15 break and announce themselves at that
 16 time.
 17 MR. BEGLEITER: I'll do that.
 18 The reason why I got cut off, I don't
 19 think the witness is speaking into a
 20 microphone, not being picked up by the
 21 microphone. I was trying to see if I
 22 could get a better way of hearing. I
 23 apologize for the disruption. I would
 24 ask that maybe he speak a little
 25 louder.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 MR. KELLER: Hey, Bob, it's
 3 Jeff. I'm just going to put the
 4 microphone closer -- the Polycom
 5 closer to you -- to the witness so you
 6 can hear. Let's carry on.
 7 BY MR. KELLER:
 8 Q. You said that typically you're
 9 looking -- the regulatory folks are looking
 10 for noninferiority. Can you define what you
 11 mean by that?
 12 A. Yeah. Noninferiority would be
 13 noninferiority of say, for example, a
 14 seroconversion rate. And if a vaccine A has
 15 a seroconversion rate of X and vaccine B
 16 which contains supposedly the same components
 17 or is supposed to elicit the same protection
 18 as a seroconversion rate; B, the
 19 noninferiority would be defined by immunizing
 20 people, measuring the antibodies, creating
 21 the difference between the seroconversion
 22 rates and building a confidence interval
 23 around the differences in seroconversion rate
 24 and postulating that. That is not greater
 25 than a given number. For example, 10 percent

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 or 5 percent, whatever is appropriate. That
 3 would often be the criterion for declaring
 4 that something is noninferior and an
 5 extension of that similar, even though what's
 6 really being tested is not inferiority, that
 7 could apply to concomitant use in which you
 8 give it with another vaccine or it could
 9 sometimes, more rarely, but sometimes also
 10 apply to the de novo licensure of the
 11 vaccine.
 12 Q. When you're talking about -- you
 13 mentioned a 4-by-4 table as part of a
 14 concordance analysis. Can you define what you
 15 mean by that?
 16 A. Just a table that classifies
 17 the positives by one assay, the positives by
 18 the other assay, the negatives by one assay,
 19 the negatives by the other assay and how that
 20 overlaps.
 21 Q. And how are those -- for
 22 purposes of comparing, for example, an ELISA
 23 to a plaque reduction neutralization assay,
 24 how would you -- is that a typical form you
 25 would expect to see in a concordance analysis

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 of those two assays?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 THE WITNESS: Yes, something
 6 like that. You would find some kind
 7 of an analysis that would tell you to
 8 which extent the assays not so much
 9 measure the same thing as classify
 10 people the same way, which is
 11 concordance.
 12 BY MR. KELLER:
 13 Q. So when they classify the same
 14 way or they discord it in the way they
 15 classify things, have you ever worked on a
 16 concordance assay between a plaque reduction
 17 neutralization and an ELISA in your --
 18 MR. SANGIAMO: Object to the
 19 form.
 20 BY MR. KELLER:
 21 Q. -- professional experience over
 22 30 years?
 23 A. I have not really run the assay
 24 lab, so I have not worked on any concordance
 25 assays. I have, of course, seen them.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. When you say you've seen them,
 3 can you describe how you came about to see
 4 them? Let me just strike that.
 5 What do you mean by see them?
 6 A. I've seen the results of
 7 whatever the lab did to provide the data and
 8 then I sometimes try to understand them.
 9 Q. And these 4-by-4 tables, how are
 10 they useful?
 11 A. Well, they tell you what
 12 percentage of results are the same and what
 13 results are different, what percentage are
 14 different in a classification assay, in a
 15 classification exercise I should say. So you
 16 find out whether an assay, two assays
 17 classify things the same way. You would not
 18 expect them generally to do that exactly. In
 19 some cases they do it pretty well and other
 20 cases not so much.
 21 Q. And for the ones that you've
 22 reviewed with regard to a plaque reduction
 23 neutralization assay and an ELISA, have you
 24 ever seen one done for the mumps virus -- mumps
 25 vaccine?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Yes. Yes.
 3 Q. So you've seen a concordance
 4 analysis comparing a plaque reduction
 5 neutralization assay and an ELISA assay?
 6 A. Yes.
 7 Q. Do you recall seeing a 4-by-4
 8 chart for that?
 9 A. Yes, I think I do, but I don't
 10 remember the details.
 11 Q. In that assay, do you recall --
 12 why would the percentages of discordant
 13 results in that assay be important?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: Well, because they
 17 give you a general idea whether the
 18 classification is the same.
 19 BY MR. KELLER:
 20 Q. When you say "the classification,"
 21 what do you mean by classification?
 22 A. Of positives and negatives in
 23 the assay.
 24 MR. SANGIAMO: Jeff, we've been
 25 going about an hour and ten minutes.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 If you reach a good breaking point --
 3 MR. KELLER: We can take a break.
 4 VIDEOGRAPHER: Off the record at
 5 10:13. This will end disc number one.
 6 - - -
 7 (A recess was taken.)
 8 - - -
 9 VIDEOGRAPHER: Back on the
 10 record at 10:25. Beginning of disc
 11 number two.
 12 BY MR. KELLER:
 13 Q. Dr. Schodel, when you moved from
 14 the clinical -- the director of clinical
 15 vaccine research in Europe to the executive
 16 director of vaccine integration, did you
 17 physically move to the United States?
 18 A. Yes.
 19 Q. And that was in November of
 20 2000, around there?
 21 A. Yes.
 22 Q. And when you -- and you
 23 testified earlier that your job duties didn't
 24 change substantially, just that you had more
 25 supervisory responsibilities when you went

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 from the executive director of vaccine
 3 integration to executive director of biologics
 4 in vaccine clinical research. Is that
 5 correct?
 6 MR. SANGIAMO: Object to the
 7 form.
 8 THE WITNESS: I don't think I
 9 said that.
 10 BY MR. KELLER:
 11 Q. Let me ask you the question.
 12 Did your duties change when you changed
 13 positions?
 14 A. When I came to the US, I --
 15 yes, my duties did change. I no longer had
 16 the EU clinical trials. I still was involved
 17 with the joint venture but much less
 18 frequently. And I had this vaccine
 19 integration role that I described to you
 20 previously, which I did not have before.
 21 Q. You also testified that you had
 22 some role with respect to the end expiry study
 23 for the mumps vaccine. Correct?
 24 A. Did I have a role? No, I did
 25 not have a direct role in that study at all.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 I have not designed it. So, no, I did not
 3 have a direct role. But some of the people
 4 at points reporting to me had a direct role.
 5 Q. And then they would report to
 6 you what was happening with that study?
 7 A. Among other studies, yes.
 8 Q. With particular to that end
 9 expiry study, did they ask you for any of your
 10 advice?
 11 A. In all probability, yes.
 12 Q. And did you review any
 13 documentation related to that study?
 14 A. Probably, yes.
 15 Q. Did you have any -- did you have
 16 any role whatsoever before you moved from
 17 Europe to the United States on that end expiry
 18 study?
 19 A. I have a vague recollection
 20 of -- as a direct role, no. I have a vague
 21 recollection of discussions during the time I
 22 was in Europe for Merck but not in the
 23 interim periods. Neither information nor any
 24 role.
 25 Q. And so when you're -- when you

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 came to the US in this executive director of
 3 vaccine integration position, did you stop
 4 having responsibilities with regard to vaccine
 5 clinical research?
 6 A. No. I still had responsibility
 7 for vaccine clinical research but primarily
 8 at that particular time, initially, primarily
 9 on varicella-containing vaccines.
 10 Q. That was part of the ProQuad
 11 application?
 12 A. ProQuad, Zostavax, yes. And
 13 varicella itself, Varivax.
 14 Q. You said that you worked for the
 15 joint venture in Europe for some of the -- did
 16 you work on the joint venture in getting the
 17 MMR vaccine approved in Europe?
 18 A. Certainly not the initial
 19 approval because that had been approved way
 20 before I came. But in subsequent approvals I
 21 may have occasionally been a part of the
 22 discussions with the joint venture. Most
 23 likely because I was on the oversight
 24 committee, so called JDVMC.
 25 Q. And so the -- are you aware that

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Merck ultimately changed its label with regard
 3 to its end expiry potency?
 4 A. Yes.
 5 Q. Okay. Do you know whether or
 6 not they changed a label with regard to its
 7 end expiry potency in Europe as well?
 8 A. I don't remember. But there is
 9 a compendial specification in Europe.
 10 Q. In that compendia, do you know
 11 if that was changed similar to what was done
 12 in the US in terms of end expiry potency?
 13 A. Not to my knowledge.
 14 Q. Do you recall submitting
 15 the results of Protocol 007 -- let me strike
 16 that.
 17 The end expiry study we're
 18 talking about, you understand to be Protocol
 19 007. Correct?
 20 A. Yes.
 21 Q. When I say "Protocol 007," you
 22 understand that to be the end expiry study.
 23 Correct?
 24 A. Yes.
 25 Q. So Protocol 007, do you know if

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 that was ever submitted to the EMA for
 3 purposes of changing the label?
 4 A. You have two parts of the
 5 question.
 6 Q. Let me start over. I'll make it
 7 simpler.
 8 Do you know if Protocol 007 was
 9 ever reported to the EMA?
 10 A. It would have been reported,
 11 yes.
 12 Q. Why would it have been reported?
 13 A. Because there is a general -- I
 14 think it might even be a law that the -- or
 15 at least there's guidance that any clinical
 16 studies with licensed vaccines have to be
 17 reported.
 18 Q. Do you know what the CDC is?
 19 A. Excuse me?
 20 Q. The CDC?
 21 A. Yes, I do know what the CDC is.
 22 Q. Did you have any -- did you ever
 23 have any communication with the CDC?
 24 A. Yes.
 25 Q. In what context?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. For example, the ACIP.
 3 Q. Did you ever speak in front of
 4 the ACIP?
 5 A. Yes, I have asked questions
 6 there for sure.
 7 Q. In regard to the MMR vaccine?
 8 A. No, I don't think so.
 9 Q. Did you ever have any
 10 conversations with the CDC regarding Protocol
 11 007?
 12 A. No, I don't remember that
 13 either.
 14 Q. Do you recall Merck ever
 15 reporting the results of Protocol 007 to the
 16 CDC?
 17 A. They were published, so I guess
 18 that certainly -- they certainly could have
 19 read them. Whether they were independently
 20 reported to the CDC, I wouldn't see why, but
 21 I don't know.
 22 Q. Where were the results of the
 23 Protocol 007 published?
 24 A. I don't remember, but it's -- I
 25 think they were published.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. And you understand that Protocol
 3 007 had reported on two different assays.
 4 Correct?
 5 A. Yes. Correct.
 6 Q. One assay was the ELISA?
 7 A. Yes.
 8 Q. The other assay was a plaque
 9 reduction neutralization assay?
 10 A. Yes.
 11 Q. That PRN -- when I say PRN, you
 12 understand that to be plaque reduction
 13 neutralization assay?
 14 A. Yes.
 15 Q. That PRN assay had been
 16 modified. Are you aware of how the assay was
 17 modified?
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: Not in all detail,
 21 but I do remember that the FDA had
 22 urged Merck to run an assay that was
 23 different in format than the assay
 24 they were at that time running.
 25 BY MR. KELLER:

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. In this -- were you at that
 3 meeting when that was discussed?
 4 MR. SANGIAMO: Object to the
 5 form.
 6 THE WITNESS: I don't remember.
 7 BY MR. KELLER:
 8 Q. You say that the assay was
 9 modified. Do you remember whether or not it
 10 was modified with the use of rabbit anti-IgG,
 11 antihuman -- strike that.
 12 Do you recall whether the PRN
 13 assay that was modified was modified with the
 14 use of adding rabbit human IgG?
 15 A. That is my understanding now,
 16 but I didn't remember that quite frankly. I
 17 wasn't sure whether it was that or a
 18 complement anti-IgG.
 19 Q. And complement is different from
 20 rabbit anti-IgG?
 21 A. Yes, it is. Yes, it is.
 22 Q. Have you ever heard of anybody
 23 using rabbit antihuman IgG in a plaque
 24 reduction neutralization assay?
 25 A. Yes.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. Where did you hear that from?

3 A. It's in the scientific literature.

4 Q. When was that literature

5 written?

6 A. It's old. I think it comes out

7 of NIH or FDA. I don't remember anymore.

8 Q. That was done in the early '70s.

9 Does that make --

10 A. Probably right.

11 Q. Do you recall any -- had Merck

12 ever used this method of using a rabbit

13 antihuman IgG?

14 A. I don't know.

15 Q. You don't know. Have you ever

16 seen any other manufacturer use it?

17 A. I have been told that it has

18 been used by other manufacturers, but I don't

19 remember seeing it.

20 Q. Who told you that?

21 A. I don't remember.

22 Q. Was it GlaxoSmithKline in their

23 MMR vaccine that they used rabbit anti-IgG?

24 A. I think they did, yes, but I'm

25 not sure.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. Do you know how -- when did you

3 learn about this?

4 A. I don't know. I mean, it could

5 have been through a publication, it could

6 have been through hearsay.

7 Q. Do you recall ever speaking to

8 somebody at GlaxoSmithKline regarding the use

9 of rabbit anti-IgG in a plaque reduction

10 neutralization assay?

11 A. No.

12 Q. Have you ever -- did you ever

13 look at the validation documents regarding the

14 PRN assay in Protocol 007?

15 A. The Merck one, yes.

16 Q. Do you recall reviewing the

17 analysis of what impact the rabbit antihuman

18 IgG had on that assay?

19 A. No.

20 Q. Are you familiar what effect the

21 rabbit antihuman IgG does have on neutralization?

22 A. Not in detail.

23 Q. What's your understanding?

24 A. I would have to speculate. So

25 it's not very useful.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. Is it based on your 30 years'

3 experience working with clinical studies

4 including plaque reduction neutralization

5 assays and ELISA assays?

6 MR. SANGIAMO: Object to the

7 form.

8 BY MR. KELLER:

9 Q. We're entitled to your best

10 understanding.

11 MR. SANGIAMO: But not speculation.

12 Right?

13 BY MR. KELLER:

14 Q. Not speculation.

15 A. Well, I couldn't offer anything

16 but speculation because at the end of the day

17 I have not run any assays with the addition

18 or without the addition of IgG. So I

19 wouldn't know the effect.

20 Q. Let me ask you differently. Do

21 you recall any discussions -- do you recall

22 reviewing any documentation at Merck that

23 criticized the use of the rabbit anti-IgG in

24 that assay?

25 A. No, not specifically.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. Do you recall any -- you say

3 not -- what about generally?

4 A. Well, what do you mean with

5 generally? I mean --

6 Q. Do you recall any documents that

7 generally --

8 A. I said -- I was answering

9 specifically your question whether I recall

10 any documentation on the use of rabbit

11 anti-IgG. And, no, I do not.

12 Q. You said specifically. I just

13 want to know --

14 A. That was the specificity.

15 Not -- I mean, do I recall assays on --

16 discussions on PRN, yes. Do I recall

17 specifically the use of anti-IgG? No. In

18 fact, I didn't even remember it until

19 recently.

20 Q. Gotcha. Do you recall ever

21 seeing any -- having any discussions at Merck

22 where they -- where somebody criticized the

23 use of anti-IgG?

24 A. It's the same -- it's sort of

25 the same difficulty, no, not in that way.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. And do you recall any discussions

3 about the use of rabbit anti-IgG, its effect

4 on the PRN assay?

5 A. No.

6 Q. You said that you reviewed some

7 information, scientific information that was

8 published a long time ago regarding the use of

9 rabbit anti-IgG in a plaque reduction

10 neutralization assay. Do you recall gaining

11 any understanding other than that publication?

12 MR. SANGIAMO: Object to the

13 form.

14 BY MR. KELLER:

15 Q. Do you understand my question?

16 A. I'm not sure -- I'm not sure if

17 I do.

18 Q. I'll rephrase it then. Other

19 than the review of that early scientific paper

20 that you testified to earlier regarding the

21 use of rabbit anti-IgG in a plaque -- in a PRN

22 assay, do you recall gaining any understanding

23 other than that paper from any other source?

24 MR. SANGIAMO: Object to the

25 form.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 THE WITNESS: As I said, I

3 specifically did not have -- I don't

4 remember having specific discussions

5 about the use or nonuse of rabbit IgG

6 in the assay, I mean, as opposed to

7 the assay.

8 BY MR. KELLER:

9 Q. Based on your 30 years'

10 experience in running and overseeing clinical

11 studies, do you have an understanding how the

12 use of rabbit antihuman IgG would affect a

13 plaque reduction neutralization assay?

14 A. Well, in a general sense,

15 adding a factor to an assay might increase

16 its sensitivity. It might decrease its

17 robustness or increase it. So it could go

18 either way.

19 Q. When you say "sensitivity," what

20 do you mean by that?

21 A. It's the ability to pick up

22 small amounts of antibody from a background.

23 Q. Gotcha. And when you say

24 "robustness," what do you mean by that?

25 A. The repeatability so the

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 other -- in other words, if you run it

3 several times, do you get the same value, is

4 it -- does it have a high standard deviation

5 or not.

6 Q. How would the rabbit antihuman

7 IgG affect the robustness?

8 A. It's a biologic reagent, so one

9 of the ways it would potentially affect it is

10 that it could vary over time.

11 Q. Would it have any impact on --

12 do you understand the term "specificity"?

13 A. Yes, I do.

14 Q. And with respect to specificity,

15 is -- do you understand the term as it's to be

16 used in a PRN assay?

17 A. Yes.

18 Q. What's your understanding of

19 specificity with respect to --

20 A. It's the ability to distinguish

21 between a signal that is caused by what you

22 want to measure, antiviral immune response as

23 opposed to something else, something that is

24 in the serum, something that could be against

25 another virus or whatever.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. So specificity for a plaque

3 reduction neutralization assay, you would be

4 looking at whether or not the neutralization

5 was caused by something other than the -- in

6 the case of the mumps assay, the mumps vaccine

7 versus some other -- let me start that over.

8 In the case of a plaque

9 reduction neutralization assay, when you look

10 at specificity, if you're testing mumps, you'd

11 want to make sure that the neutralization was

12 caused by the mumps vaccine as compared to

13 some other antibody or any other effect.

14 Correct?

15 MR. SANGIAMO: Object to the

16 form.

17 THE WITNESS: That's true for

18 any assay. You always want to make

19 sure that you're actually measure what

20 you want to measure and not something

21 that is influenced by something else.

22 It could be influenced by serum alone

23 or by other viruses or by schmutz. I

24 mean, it's the -- the possibilities

25 are endless. So whatever you're

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 measuring, you want to make sure that
 3 you reliably measure what you want to
 4 measure.
 5 BY MR. KELLER:
 6 Q. So in a plaque reduction
 7 neutralization -- like, for example, in
 8 Protocol 007 when they did a plaque reduction
 9 neutralization assay using the mumps vaccine,
 10 when they -- do you know whether or not they
 11 validated and tested whether or not that assay
 12 was specific and what percentage of
 13 specificity it had?
 14 A. I do not remember that the
 15 percentage of specificity was specifically
 16 analyzed in the validation protocol. I do
 17 remember that the assay was validated and the
 18 validation was accepted by the FDA.
 19 Q. Do you know whether or not -- do
 20 you recall any discussions at Merck regarding
 21 the specificity of the -- of Protocol 007's
 22 PRN assay?
 23 A. Vaguely. As with any assay,
 24 you would have -- you would have potentially
 25 specificity issues.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. Do you recall if there were
 3 specificity issues with this particular PRN
 4 assay in Protocol 007?
 5 A. Well, I don't know that the
 6 specificity, as I said, has ever been
 7 analyzed, so I can't tell you for sure.
 8 Q. Do you recall there ever --
 9 Merck ever doing any analysis as to whether or
 10 not the use of the rabbit antihuman IgG had
 11 any impact on the specificity of the PRN assay
 12 in Protocol 007?
 13 A. No, I do not.
 14 Q. Do you ever have an opinion
 15 yourself about that?
 16 A. It would be speculation because
 17 I wouldn't have a comparison so I wouldn't
 18 know what specificity to expect in comparison
 19 because the analysis hasn't been done, so I
 20 really can't tell you.
 21 Q. I see. Do you have any, based
 22 on your 30 years of experience, have any
 23 understanding as to whether or not the use of
 24 the rabbit antihuman IgG could have an impact
 25 on specificity of that assay used in Protocol

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 007?
 3 A. As any reagents in an assay, it
 4 likely would have an impact on specificity.
 5 Q. But you're not aware of Merck
 6 ever analyzing what that impact was?
 7 A. No. And I certainly don't know
 8 if they have done it. I just don't know.
 9 Q. You just don't recall?
 10 A. No, I -- well, yeah, I don't
 11 recall it, I don't know.
 12 Q. Would you --
 13 A. I mean, it's possible that
 14 they've done it and they haven't told me.
 15 It's always possible that I forgot it, but I
 16 don't know.
 17 Q. Would you be surprised with the
 18 use of the rabbit antihuman IgG that they
 19 wouldn't have tested this specificity --
 20 MR. SANGIAMO: Object to the
 21 form.
 22 BY MR. KELLER:
 23 Q. -- since you're adding that into
 24 a -- into the test that you're doing?
 25 MR. SANGIAMO: Object to the

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 form.
 3 THE WITNESS: Would I be
 4 surprised? I think as part of the --
 5 as part of the assay analysis, it
 6 might be reasonable to do it. I would
 7 not be too surprised if that
 8 particular analysis had not been done.
 9 BY MR. KELLER:
 10 Q. Have you, as part of your
 11 research in looking -- strike that.
 12 Do you recall there being any
 13 discussion at Merck that the use of the rabbit
 14 antihuman IgG had a significant fold increase
 15 in the neutralization of that assay?
 16 A. Well, again, I've already said
 17 that several times. I don't -- I do remember
 18 that Merck, under guidance from the FDA,
 19 tried to make particularly sensitive assay,
 20 but I don't remember any discussion as to the
 21 IgG.
 22 Q. Sure.
 23 A. So I just don't know.
 24 Q. Gotcha.
 25 A. I was not involved in that.

25 (Pages 94 - 97)

<p style="text-align: right;">Page 98</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 Q. In your 30 years of experience,</p> <p>3 would it be a concern to you if the use of</p> <p>4 rabbit antihuman IgG would increase the</p> <p>5 neutralization by a hundredfold?</p> <p>6 MR. SANGIAMO: Object to the</p> <p>7 form.</p> <p>8 THE WITNESS: No, because all</p> <p>9 the assays are relative and have to be</p> <p>10 validated in and by themselves. I</p> <p>11 mean, a hundredfold increase of</p> <p>12 something, you know, PCR assays are</p> <p>13 sometimes a lot more sensitive than</p> <p>14 other assays, but it might have less</p> <p>15 specificity because it's easier prone</p> <p>16 to contamination. So in principle,</p> <p>17 no.</p> <p>18 BY MR. KELLER:</p> <p>19 Q. So would you expect when Merck</p> <p>20 validated the PRN assay with the antihuman</p> <p>21 IgG, that they would have somehow tried to</p> <p>22 control for that affect on specificity?</p> <p>23 MR. SANGIAMO: Object to the</p> <p>24 form.</p> <p>25 THE WITNESS: Well, you're</p>	<p style="text-align: right;">Page 100</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 assays in the past, you've overseen those</p> <p>3 assays used in other context. Correct?</p> <p>4 A. No, not correct.</p> <p>5 Q. You've never reviewed the</p> <p>6 protocols of the plaque reduction neutralization</p> <p>7 assay before?</p> <p>8 A. They were not run in my lab. I</p> <p>9 have -- I mean, in the course of my life,</p> <p>10 I've seen protocols. I've seen validation</p> <p>11 protocols and I've seen validation results.</p> <p>12 But -- and I've read them. But I wasn't the</p> <p>13 one who wrote them or put them in place.</p> <p>14 Q. Gotcha. And as part of your</p> <p>15 consulting duties since you left Merck, have</p> <p>16 you ever discussed with one of your clients</p> <p>17 these are the plaque reduction neutralization</p> <p>18 assays?</p> <p>19 A. With several, yes.</p> <p>20 Q. Did you review those protocols?</p> <p>21 A. No, not in detail. In general.</p> <p>22 My advice is usually more strategic.</p> <p>23 Q. In any of the plaque reduction</p> <p>24 neutralization assays, protocols or</p> <p>25 discussions that you've had in your 30 years</p>
<p style="text-align: right;">Page 99</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 assuming that they have analyzed and</p> <p>3 indeed -- and that specificity and</p> <p>4 then they would have to control for it</p> <p>5 because it wasn't what was expected.</p> <p>6 So there's too many assumptions in</p> <p>7 there.</p> <p>8 BY MR. KELLER:</p> <p>9 Q. Gotcha. Let me ask you</p> <p>10 differently then. Do you know whether or not</p> <p>11 Merck used a serum negative control versus a</p> <p>12 mock control in their PRN assay in Protocol</p> <p>13 007?</p> <p>14 A. No.</p> <p>15 Q. Do you know what difference that</p> <p>16 would make with respect to the use of rabbit</p> <p>17 anti-IgG in terms of determining whether or</p> <p>18 not the use of that addition would change the</p> <p>19 specificity of the vaccine -- of the assay?</p> <p>20 MR. SANGIAMO: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: No, I don't.</p> <p>23 BY MR. KELLER:</p> <p>24 Q. When you have overseen the</p> <p>25 running of plaque reduction neutralization</p>	<p style="text-align: right;">Page 101</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 of experience, have you ever discussed whether</p> <p>3 or not to use a mock serum control versus a</p> <p>4 serum control?</p> <p>5 A. Yes.</p> <p>6 Q. What is the difference, reason</p> <p>7 why you'd use one or the other?</p> <p>8 A. In fact, I've discussed using</p> <p>9 various kinds of mock serum or serum</p> <p>10 controls. They all have their pros and cons.</p> <p>11 A none negative serum control has the</p> <p>12 advantage that it is in the right matrix</p> <p>13 serum that you want to measure in, but it</p> <p>14 doesn't necessarily represent all sera. A</p> <p>15 mock depleted serum control in which the</p> <p>16 specific antibody has been depleted by</p> <p>17 absorption has the advantage that you're</p> <p>18 measuring in a matrix in which it would</p> <p>19 normally be the analyte but it has been</p> <p>20 artificially removed. It's also artificial</p> <p>21 but it has some other advantages. Then there</p> <p>22 are other mock controls which appear to mimic</p> <p>23 the composition of serum without being serum</p> <p>24 themselves, for example, by adding albumin</p> <p>25 and other things. They have the advantage</p>

26 (Pages 98 - 101)

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 2 that they're highly reproducible. But the
 3 disadvantage that they're not as close to all
 4 the kinds of things we do know in serum.
 5 So there's all kinds of
 6 different ways of creating these controls.
 7 I've seen many of them applied. I don't
 8 recall any major problems with any of them as
 9 such other than that with any of these
 10 controls containing serum, it's difficult to
 11 figure out exactly what you have to control
 12 for because sera are variable. In other
 13 words, you have one control, but you can't
 14 control for all the things that are in sera
 15 other than specific antibodies.
 16 Classic one is that, for
 17 example, if a serum is bloody, you generally
 18 don't use it because it has live erythrocytes
 19 in it. That influences some assays, not
 20 others. So that's a wide field. They have
 21 to be appropriate for the assay. It doesn't
 22 necessarily mean that one is better than the
 23 other.
 24 Q. Let me ask you a question about
 25 that in a little more detail. Do you have any

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 understanding as to how rabbit antihuman IgG
 3 would interact with serum that may have other
 4 antibodies in it?
 5 A. No, I don't.
 6 Q. You don't. Do you recall any
 7 discussion at Merck regarding how the rabbit
 8 antihuman IgG would interact with serum?
 9 A. I simply don't recall any
 10 discussions with rabbit anti-IgG.
 11 Q. Fair enough. Fair enough.
 12 Let me ask you a question
 13 about --
 14 A. By the way, it's because I see
 15 the transcription, it's rabbit as in the
 16 animal, not rabid as in the infected --
 17 sorry.
 18 Q. Let me ask you a question a
 19 little more scientific. What does antihuman
 20 IgG bind to?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: It binds to human
 24 IgG, immunoglobulin G, an epitome on
 25 immunoglobulin G or several epitomes

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 2 on -- it depends on whether it's a
 3 monoclonal antibody or polyclonal
 4 serum, it will bind to different
 5 things on immunoglobulin G.
 6 BY MR. KELLER:
 7 Q. Does it also bind to other
 8 antibodies?
 9 A. That's not something that I can
 10 answer in general because it depends on how
 11 it's been made and how it's been absorbed.
 12 So if -- depending on whether it is made with
 13 IgG as the immunizing principle and it's not
 14 cross absorbed, it might bind to other
 15 antibodies or not. It really depends on what
 16 it is.
 17 Q. What human antibodies have IgG
 18 in it, what percentage, if you know?
 19 A. It's the predominant antibody
 20 in serum.
 21 Q. So antihuman IgG would bind --
 22 let me back up for a second. Let me come back
 23 to that in a minute. Let's keep pushing
 24 forward. Let me ask you a couple of
 25 questions.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 In a PRN assay, you've testified
 3 that specificity is important to make -- to
 4 make sure that the neutralization that you're
 5 getting in that assay is actually caused by
 6 the antigen that you're testing for. Correct?
 7 A. That's correct.
 8 MR. SANGIAMO: Object to the
 9 form.
 10 BY MR. KELLER:
 11 Q. So is there a standard or a rule
 12 of thumb that you're aware of for plaque
 13 reduction neutralization assays as to what
 14 you'd want to see in terms of specificity?
 15 A. No. No.
 16 Q. If there was only 10 percent
 17 specific, so 90 percent of what it was
 18 neutralizing wasn't the antigen you were
 19 testing, that would be a concern, wouldn't
 20 that?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: Well, it depends
 24 on the circumstances. If that's as
 25 good as you could get, then you would

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2 make sure that the 10 percent are

3 always the same 10 percent. But

4 that's a bit of an extreme example.

5 BY MR. KELLER:

6 Q. Well, in the Protocol 007 PRN,

7 they are reporting in seroconversion,

8 correct -- let me strike that.

9 For Protocol 007, do you know

10 what the endpoint was for the PRN assay?

11 A. It was -- I don't have a

12 perfect recollection. I think it was the

13 seroconversion rate, and the major endpoint

14 that I remember, because that's why the

15 protocol was done, was the comparison of the

16 seroconversion rates between the different

17 lower titered cells --

18 Q. So how would specificity --

19 A. -- to the control.

20 Q. Strike that. Strike that.

21 How would specificity affect

22 seroconversion rates in this particular

23 Protocol 007 PRN assay?

24 A. That's a really interesting

25 question. I can't really answer it, but it

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2 would certainly not affect the comparison

3 because you would expect the specificity to

4 be always the same. Since the major point

5 was the comparison, it wouldn't really affect

6 the major point of the trial.

7 Q. Well, in Protocol 007 they

8 tested the market product potency.

9 A. Right.

10 Q. Correct?

11 A. Right.

12 Q. They tested the intermediate

13 potency?

14 A. Right.

15 Q. And low potency. Correct?

16 A. Right.

17 Q. So do you recall there being a

18 concern that in testing Protocol 007 through a

19 PRN assay, that the seroconversion rate that

20 reported would possibly impact the label for

21 the seroconversion reported in the label?

22 A. No.

23 Q. So is it fair to say that the

24 specificity of -- in the Protocol 007's PRN

25 assay could impact the percentage that's

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2 identified as seroconversion?

3 A. That's more the sensitivity

4 that would impact that rather than the

5 specificity, as long as the specificity is

6 always kept at the same level.

7 Q. Right. But if you're test -- if

8 the purpose of Protocol 007 -- let me ask you,

9 was -- the endpoint of Protocol 007 was to

10 test to identify a seroconversion rate.

11 Correct?

12 A. The endpoint was to make sure

13 that the lower titered cells would have at

14 least as good as be noninferior to the

15 marketed control.

16 Q. But my question is, if the

17 seroconversion rates that are being tested, if

18 that assay is -- has a specificity that is

19 low, let's use 50 percent as a number, it's in

20 the middle, if 50 percent of the -- if the

21 assay is only 50 percent specific, that means

22 50 percent of the neutralizing --

23 neutralization that occurs is based on something

24 other than the mumps vaccine. Correct?

25 MR. SANGIAMO: Object to the

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2 form.

3 THE WITNESS: You have to see

4 that in the design. So I don't know

5 how a low specificity would affect the

6 seroconversion rates because that's

7 more determined by the sensitivities I

8 said. And as long as the specificity

9 is the same in all three cells, you

10 would still have a valid comparison of

11 whether they were noninferior.

12 So here in the design and in the

13 question of this protocol, I'm not

14 concerned about the absolute

15 seroconversion rate. I'm concerned

16 about which -- does it fall off

17 somewhere. If you give less than you

18 normally give, would that make it less

19 potent. It's a different comparison,

20 therefore, specificity doesn't in my

21 mind directly influence it.

22 BY MR. KELLER:

23 Q. I see. But it does directly

24 influence whether or not that seroconversion

25 number would -- let me ask you a question.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 In the original Hilleman assays
 3 that were conducted where they approved the
 4 mumps vaccine, these used seroconversion as a
 5 means to show how well the vaccine would work
 6 in protecting kids from getting sick from the
 7 disease. Correct?
 8 A. Well, it was sort of the other
 9 way around. They had at that time because
 10 mumps was frequent, still the luxury of doing
 11 controlled studies in the population that was
 12 exposed to mumps, and primarily what they
 13 measured was whether the vaccine would
 14 prevent cases of mumps or not. Sorry. And
 15 then, of course, they also measured
 16 immunogenicity, and it turned out that the
 17 seroconversion was probably even
 18 underestimating the level of protection that
 19 they saw. But there was never a clear
 20 correlate established between the two.
 21 Q. So if Merck -- do you know
 22 whether or not Merck ever represented -- let
 23 me strike that.
 24 So your -- just so I'm clear,
 25 your testimony is that specificity wouldn't

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 matter in this particular assay because you're
 3 only testing whether or not the lower doses
 4 matched seroconversion in the higher doses.
 5 Correct?
 6 A. It wouldn't matter for the
 7 outcome of the study, yes.
 8 Q. I see. Would it matter if the
 9 outcome was determine whether or not the kids
 10 would get -- be protected by the vaccine?
 11 A. Well, first of all, that's not
 12 the question of the study. And secondly, no,
 13 because an assay in itself does not -- does
 14 not -- especially if no correlate has been
 15 established, does not give you a certainty
 16 that you're protected or not. That's the
 17 difficulty with something where no correlate
 18 has been established. One of the reasons it
 19 has not been established is that there is not
 20 a known titer at which you have absolutely no
 21 certainty of -- absolutely no chance of
 22 getting mumps. You can have antibodies and
 23 you can still get mumps.
 24 Q. So if there was a correlation
 25 between a plaque reduction neutralization

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 assay and protection from disease, then would
 3 specificity matter in that assay?
 4 MR. SANGIAMO: Object to the
 5 form.
 6 THE WITNESS: That's too
 7 absolute a question. In other words,
 8 in a comparison it still wouldn't
 9 matter. In a comparison of two things
 10 that are different and used as just
 11 for the sake of the comparison. So
 12 for the purposes of 007 that wouldn't
 13 matter.
 14 BY MR. KELLER:
 15 Q. Would it be something that would
 16 be important for a regulator to know?
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: If the regulator
 20 wanted to ask that question, obviously
 21 it would be important for them to
 22 know, but that's not a question that I
 23 remember ever having been asked.
 24 BY MR. KELLER:
 25 Q. You don't think it's important

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 whether or not when you're looking at
 3 something that's correlated to immunity,
 4 correlated to protection of a disease by a
 5 vaccine, whether or not in a plaque reduction
 6 neutralization assay, in fact, that a
 7 percentage of what's being neutralized that is
 8 used to report seroconversion was based on
 9 something other than the vaccine?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: I don't understand
 13 your question.
 14 BY MR. KELLER:
 15 Q. Sure. I'll back up a second,
 16 try to break it down for you.
 17 Your testimony specificity is
 18 irrelevant -- let me strike that.
 19 Is specificity -- was
 20 specificity irrelevant in Protocol 007, the
 21 PRN assay?
 22 A. Largely, yes, because it's a
 23 comparison. So the absolute -- and I don't
 24 know the exact specificity, that's why I
 25 can't really answer it. But because of the

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2 comparative nature of the study, it was not a
3 study to predict the likelihood of cases of
4 mumps occurring but a study to compare
5 different potencies of mumps. For that
6 particular purpose it was irrelevant.
7 Q. Do you know whether or not Merck
8 ever represented that its Protocol 007 study
9 was correlated to protecting kids from getting
10 sick?
11 A. No, I don't remember that. And
12 I -- no, I don't.
13 Q. Would that change your testimony
14 as to whether or not specificity of the PRN
15 assay was relevant?
16 MR. SANGIAMO: Object to the
17 form.
18 THE WITNESS: No, it would not.
19 BY MR. KELLER:
20 Q. Still not?
21 A. It would not because the same
22 lack of specificity would be true for all --
23 would be true for all cells. In other words,
24 if they behaved the same, there's no reason
25 to expect that they would correlate

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2 differently with the likelihood of getting
3 disease.
4 So in other words, even if the
5 assay wasn't perfect, as no assay is, if they
6 were the same in all three cells, even if
7 there was a correlation, the correlation
8 would still be the same for all three cells.
9 It doesn't matter. So the concept is different.
10 Q. If Merck was conducting -- let
11 me strike that.
12 If the PRN assay was going to be
13 used to set what the seroconversion rate was
14 for the label, for that purpose, would that
15 have -- would the specificity have -- be
16 important for that analysis?
17 MR. SANGIAMO: Object to the
18 form.
19 THE WITNESS: I can't really
20 answer that question. I mean, the
21 reported number in the label is a
22 number given -- that was an assay
23 result at a given time when the
24 vaccine was licensed. And at that
25 time it was truly reported as whatever

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2 it was. So I don't see how
3 specificity would be -- would enter
4 into the label.
5 BY MR. KELLER:
6 Q. Do you recall there being any
7 discussions at the time that you were at Merck
8 where there was a concern that if Merck
9 reported seroconversion rates lower than what
10 was reported in its label, that it would have
11 to reduce or change its label to reflect those
12 new results?
13 A. I don't remember a discussion
14 exactly around those lines, but I do remember
15 -- and I don't remember whether I heard them
16 myself or heard of them, discussions with the
17 FDA where the FDA expressed a desire that the
18 seroconversion rates in the label be
19 reflected by an assay that was run to test
20 the vaccine.
21 Q. Let me sort of break this down a
22 little bit. If your -- if the assay was -- if
23 you had to report the seroconversion rate that
24 was reported in the Protocol 007 in its label
25 as -- would that affect your analysis as to

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2 whether or not the specificity of what was
3 neutralized would have been relevant for that
4 analysis?
5 A. No. I don't really -- I don't
6 really see the connection. I mean, what
7 you're talking about is more sensitivity than
8 specificity.
9 Q. Well, let me break it down into
10 smaller bits. You testified earlier that
11 specificity in a plaque reduction
12 neutralization assay is identifying whether or
13 not the neutralization that occurs happens
14 from the antigen you're testing. Correct?
15 A. That's correct.
16 Q. And if a percentage of that
17 neutralization comes from something other than
18 the antigen, that means -- that's what
19 specificity is discussing. If it's 50 percent
20 specific, 50 percent of what's being
21 neutralized is caused by the antigen being
22 tested and 50 percent is being caused by
23 something else. Correct?
24 A. Yeah, that's correct.
25 Q. And so --

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2 A. But we don't have an analysis

3 that the --

4 Q. Let me just kind of go through

5 this so I understand it.

6 And so if --

7 MR. SANGIAMO: Wait a minute,

8 Jeff. He was -- let him finish with

9 his answer.

10 BY MR. KELLER:

11 Q. Are you done?

12 A. No, I wasn't. We don't have an

13 analysis that suggests that the assay had a

14 50 percent specificity to start with.

15 Q. Assume it did for the purpose of

16 this discussion. And so in that situation,

17 what effect does neutralization have on the

18 reporting of seroconversions in a plaque

19 reduction neutralization assay?

20 MR. SANGIAMO: Object to the

21 form.

22 THE WITNESS: I'm not sure I

23 understand. What effect does

24 neutral --

25 BY MR. KELLER:

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2 Q. Yeah, when a plaque reduction

3 neutralization assay reports in a

4 seroconversion, it's reporting the number of

5 plaques that have been -- that are identified

6 in a dish. Correct?

7 A. Yes.

8 Q. And so what the plaque reduction

9 neutralization assay is doing, it's looking at

10 a dish prevaccination and comparing that to a

11 dish postvaccination after a certain period of

12 time. Correct?

13 A. Right.

14 Q. So if the neutralization that

15 occurs is caused by 50 percent something other

16 than the antigen that you're testing, that

17 could have an impact on an overstate

18 seroconversion, couldn't it?

19 A. It depends on the circumstances.

20 You have to -- just to give you an example,

21 if you have -- to stay with this kind of a

22 general assumption, if you have a pre-titer

23 of say 1 to 8, and then you have a post titer

24 of 1 to 256, for example, now you take

25 50 percent of that, then you would be having

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2 a pre-titer of 1 to 4. And the pre-titer of

3 1 to 4, assuming that everything is linear,

4 would go to half of 1 to 256 or 128. That

5 would still be a seroconversion. So it

6 would -- in that case it would have no impact

7 whatsoever.

8 Q. But in the case where the --

9 A. So you're making a wrong

10 assumption. Your assumption, and I'm not

11 quite sure where that happens, but that

12 example should make it clear to you that even

13 an assay in which not all the reported

14 numbers come from the specific part of the

15 assay but there is also contribution of a

16 nonspecific part can still be highly

17 sensitive and sufficiently specific to report

18 a seroconversion rate.

19 Q. So what happens when the numbers

20 are compressed, you know, you're looking at

21 around that seroconversion cutoff, you have

22 numbers that are much closer to the cutoff,

23 that 50 percent criteria?

24 MR. SANGIAMO: Object to the

25 form.

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2 THE WITNESS: Well, again,

3 that's making too many assumptions.

4 Then they would also be -- if

5 everything was linear, they would also

6 be still linear. It would still be in

7 the same direction.

8 MR. SANGIAMO: Sorry. Let me --

9 MR. KELLER: Just so I'm clear,

10 let me --

11 MR. SANGIAMO: No, no, no. I've

12 been letting this go for a while.

13 You're asking -- Dr. Schodel is not

14 being presented as an expert witness

15 in this case. He's here as a fact

16 witness. You're asking a whole lot of

17 hypothetical questions. He's

18 answering them, I've been letting it

19 go. I think we're getting close to

20 the time where it's time to start

21 moving on.

22 BY MR. KELLER:

23 Q. Just so I'm clear, Dr. Schodel,

24 it's your view that specificity was irrelevant

25 to the Protocol 007 PRN assay?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 MR. SANGIAMO: Objection. Asked
 3 and answered.
 4 THE WITNESS: No, that's not
 5 exactly what I said. I said that for
 6 the degree of specificity, as long as
 7 it was the same or similar was
 8 irrelevant for the primary endpoint,
 9 the analysis of the comparison.
 10 MR. KELLER: Let's do this,
 11 let's -- let me mark as Exhibit 3 --
 12 - - -
 13 (Exhibit Schodel-3, Immunological
 14 Correlates of Vaccine-Derived Protection
 15 Fondation Mérieux Conference Center
 16 'Les Pensières' Veyrier-Du-Lac, France
 17 article, was marked for identification.)
 18 - - -
 19 BY MR. KELLER:
 20 Q. This is a document, an article
 21 written by you, Dr. Schodel, "Immunological
 22 Correlates of Vaccine-Derived Protection...,"
 23 and then it appears that this was presented at
 24 a conference in France. And I will not even
 25 try to give the rest of the title in French.

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 2 But do you recall comparing this?
 3 A. Yeah, this was basically a
 4 summary of that meeting.
 5 Q. Dr. Plotkin gave a lecture about
 6 correlates and surrogates. Correct?
 7 A. Uh-huh.
 8 Q. Do you recall that particular
 9 seminar?
 10 A. I've heard him -- not that
 11 particular one, but I've heard Stanley speak
 12 many times about correlates, yes.
 13 Q. In this introduction you write,
 14 "It is often not feasible and occasionally not
 15 ethically justifiable to run placebo
 16 controlled clinical trials for efficacy.
 17 Hence, correlates of vaccine induced
 18 protection have an important role in the
 19 discovery, development and life cycle
 20 management of vaccines (for example changes in
 21 the manufacturing process, concomitant use
 22 with vaccines, extension of the age range of
 23 the indication)."
 24 Do you see that?
 25 A. Yes.

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 2 Q. When you wrote that, did you
 3 believe that statement to be correct?
 4 A. Yes, I still think it's correct.
 5 Q. Under "Terminology" you write in
 6 the third paragraph, "I'd suggest that the
 7 term immunological correlate of protection is
 8 reserved for such correlates where immune
 9 measures in a validated assay have been shown
 10 to correlate with protection from infection
 11 and/or disease in controlled trials in a
 12 statistically meaningful manner."
 13 Do you see that?
 14 A. Yes.
 15 Q. Do you believe that statement to
 16 be true?
 17 A. Yes.
 18 Q. So correlates of protection,
 19 that's an important -- let me strike that.
 20 Typically you look at a
 21 correlate of protection in a situation where
 22 you can't do a clinical study because of
 23 ethical reasons. Correct?
 24 A. If one is available. You
 25 typically look at a correlate of protection

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 where a correlate of protection has been
 3 established. Sometimes you have to do it
 4 without one because there hasn't been one
 5 established.
 6 Q. So as you -- it's your testimony
 7 earlier that for MMR the only correlates of
 8 protection that you're aware of is with
 9 measles. Correct?
 10 A. That's the best established.
 11 Even that, as I pointed out, there are some
 12 issues.
 13 Q. When you say "correlate of
 14 protection," do you mean that -- is that the
 15 same as correlate of effectiveness?
 16 A. No.
 17 Q. What's the difference?
 18 A. Well, effectiveness is a
 19 concept which combines real world exposure to
 20 a drug or a vaccine and outcomes that are
 21 observed. It is usually not prospective, it
 22 can be prospective and the controls are not
 23 randomized controls. So what you look at is
 24 a population effect in people who are
 25 vaccinated as opposed -- like as an example,

<p style="text-align: right;">Page 126</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 for opposed to people who are not vaccinated.</p> <p>3 But there are many other factors why people</p> <p>4 aren't vaccinated, and so the groups are</p> <p>5 hardly ever exactly identical. So</p> <p>6 effectiveness is much less precise measure of</p> <p>7 whether a vaccine as such works or is</p> <p>8 efficacious than efficacy. It is on the</p> <p>9 other hand by some felt to be a measure of</p> <p>10 real life usefulness. But it has many, many</p> <p>11 factors that go beyond any of the things</p> <p>12 we've discussed here.</p> <p>13 Q. So have you ever seen the term</p> <p>14 correlate with efficacy?</p> <p>15 A. Yes.</p> <p>16 Q. And what does that mean based on</p> <p>17 your understanding?</p> <p>18 A. Well, that means that a</p> <p>19 laboratory measure can predict whether</p> <p>20 somebody is protected or not. In that</p> <p>21 regard, measuring that laboratory measure can</p> <p>22 help you ascertain whether a drug vaccine,</p> <p>23 whatever else will likely protect or not --</p> <p>24 likely protect or not protect against the</p> <p>25 disease. But that's measured in an efficacy</p>	<p style="text-align: right;">Page 128</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 Q. Would that surprise you as well?</p> <p>3 A. Well, depends on who made that</p> <p>4 statement.</p> <p>5 Q. If Merck made that statement.</p> <p>6 A. Somewhat. It's not an efficacy</p> <p>7 study.</p> <p>8 Q. Did you ever make that statement?</p> <p>9 A. I don't remember it, no.</p> <p>10 Q. Did you ever make the statement</p> <p>11 that Protocol 007 was a correlate of vaccine</p> <p>12 effectiveness?</p> <p>13 A. I don't think so.</p> <p>14 MR. SANGIAMO: Object to the</p> <p>15 form.</p> <p>16 BY MR. KELLER:</p> <p>17 Q. You would be surprised if you</p> <p>18 did?</p> <p>19 A. I would be surprised if I did.</p> <p>20 Q. Because correlates of vaccine</p> <p>21 effectiveness and correlates of vaccine</p> <p>22 efficacy, those are two different ways that</p> <p>23 show that a vaccine actually protect the kids</p> <p>24 from getting sick. Correct?</p> <p>25 A. In the efficacy, yes, that's</p>
<p style="text-align: right;">Page 127</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 setting. Efficacy means that you have a</p> <p>3 well-defined randomized controlled trial with</p> <p>4 enough endpoints and it's all set up in the</p> <p>5 right way.</p> <p>6 Q. Are you aware of whether or not</p> <p>7 Protocol 007 was ever described as a correlate</p> <p>8 of vaccine effectiveness?</p> <p>9 A. No --</p> <p>10 MR. SANGIAMO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: -- I'm not aware</p> <p>13 of that.</p> <p>14 BY MR. KELLER:</p> <p>15 Q. Did you ever --</p> <p>16 A. If it had been described that</p> <p>17 way, I might be a bit surprised.</p> <p>18 Q. Are you aware of Protocol 007</p> <p>19 ever being described as a correlate of vaccine</p> <p>20 efficacy?</p> <p>21 MR. SANGIAMO: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: No, I'm not aware</p> <p>24 of that.</p> <p>25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 129</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 clearly primarily the vaccine. In the</p> <p>3 effectiveness it is societal factors other</p> <p>4 than the vaccine as well so it's not as</p> <p>5 direct a measure of the vaccine.</p> <p>6 Q. Would you consider if somebody</p> <p>7 made the statement that both of those existed</p> <p>8 with Protocol 007, that that would be</p> <p>9 considered a correlative with protection?</p> <p>10 MR. SANGIAMO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: No. It was not</p> <p>13 set up to do, to measure efficacy or</p> <p>14 effectiveness. I mean, MMR is a</p> <p>15 highly efficacious and effective</p> <p>16 vaccine but the measure for that is</p> <p>17 different.</p> <p>18 MR. KELLER: Let me mark as</p> <p>19 Exhibit 4.</p> <p>20 - - -</p> <p>21 (Exhibit Schodel-4, E-mail string,</p> <p>22 Bates MRK-KRA01648951 - 01648956, was</p> <p>23 marked for identification.)</p> <p>24 - - -</p> <p>25 BY MR. KELLER:</p>

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 2 Q. Exhibit 4 is a document that
 3 bears Bates stamp numbers KRA01649851 through
 4 956, and it's a series of e-mails.
 5 Doctor, if you could take a
 6 moment to review the e-mails, it will save us
 7 time rather than me trying to read this stuff
 8 into the record. Just take a moment. Let me
 9 know when you're done.
 10 MR. SANGIAMO: It's a long
 11 e-mail thread, Jeff. No expectation
 12 he would have been done already.
 13 MR. KELLER: I understand.
 14 THE WITNESS: I think I have
 15 a -- I will see whether I may need to
 16 go back because there's a lot of stuff
 17 in there.
 18 BY MR. KELLER:
 19 Q. That's okay. I just wanted to
 20 have you -- so you have an understanding of
 21 sort the context of this e-mail. This
 22 e-mail -- there's a series of e-mails that
 23 were written before it was -- before you were
 24 e-mailed as part of this e-mail chain and
 25 instead of me going through everything that

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 2 happened before the e-mails came to you, I
 3 thought it was helpful to have you review it.
 4 But if you look on the third
 5 page, which is 1648953, there's an e-mail from
 6 Joan Staub on June 19, 1997, to Henrietta Ukwu
 7 and Barry Garfinkle and there's a series of
 8 other people on this e-mail including David
 9 Kraah, Alan Shaw, Jerry Sadoff. And this is
 10 regarding mumps issues. In here this e-mail,
 11 though you're not on this, it's in the chain
 12 of e-mails that was ultimately sent to you,
 13 there's a statement that says Henrietta -- let
 14 me back up for a second.
 15 Who is Joan Staub?
 16 A. Joan Staub was a project
 17 manager at Merck.
 18 Q. Was she a project manager on
 19 MMR II, if you recall?
 20 A. I don't remember. But since
 21 she's sending these e-mails, she had probably
 22 some project management responsibilities.
 23 Q. Who is Henrietta Ukwu?
 24 A. Henrietta Ukwu at the time was
 25 the regulatory person for vaccines at Merck.

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 2 Q. And Barry Garfinkle?
 3 A. Henrietta was on the clinical
 4 side, Barry was on the manufacturing side.
 5 He was the quality person of it. I don't
 6 know whether he was regulatory or quality for
 7 vaccines on the manufacturing side.
 8 Q. Here Joan Staub is saying,
 9 "Henrietta/Barry, The suggestion from the MMR
 10 Competitive Defense Task Force was to actually
 11 run a clinical trial with Mu at expiry since
 12 SB will be filing in Germany and is expected
 13 to come on the market in 1998."
 14 Do you see that?
 15 A. Yes.
 16 Q. This MMR competitive defense
 17 task force, were you a member of that?
 18 A. I don't remember that.
 19 Q. Do you remember what that task
 20 force job was or role or purpose?
 21 A. Probably to make sure that MMR
 22 meets all criteria and can stay on the
 23 market. Remain competitive. I don't know.
 24 Q. Do you recall there ever
 25 being -- do you recall ever seeing any

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 2 documentation from this task force?
 3 A. I'm not seeing one right here
 4 apparently. So that's the last time that I
 5 remember one. I didn't even know the thing
 6 existed.
 7 Q. Fair enough. Was it -- during
 8 the time that you were at Merck, was it
 9 Merck's practice before meetings of its
 10 committees that it would send out an agenda in
 11 a background paper what was to be discussed at
 12 that meeting?
 13 MR. SANGIAMO: Object to the
 14 form.
 15 THE WITNESS: I don't know
 16 whether I can make a general statement
 17 like that. There were all kinds of
 18 general meetings. Some meetings were
 19 very formalized, and, yes, that was
 20 done. Other meetings were very
 21 informal and, no, that was not done.
 22 BY MR. KELLER:
 23 Q. In this e-mail when it says Mu,
 24 you understand that to be mumps. Correct?
 25 A. No, it's MMR. Mu, yes. Mu is

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 2 mumps. Yeah. Okay.
 3 Q. And SB, that's Smith --
 4 A. Smith Beecham probably, yeah,
 5 sure.
 6 Q. And that's Glaxo Smith today.
 7 Correct?
 8 A. Yeah. Yeah.
 9 Q. Do you know whether or not -- so
 10 here there is a discussion here about running
 11 a clinical trial with mumps at expiry. Do you
 12 see that?
 13 A. Uh-huh.
 14 Q. Do you recall giving an opinion
 15 about what that clinical trial would look like
 16 during this time frame? I know it's a long
 17 time ago.
 18 A. No, I don't specifically
 19 remember this one. But, you know, there's
 20 a -- in general, there's always a debate if
 21 you want to know whether something works at
 22 end expiry as to whether -- how you should do
 23 that. And I -- if somebody had asked me an
 24 opinion on how to do that, I would certainly
 25 have weighed the pros and cons of doing

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 2 dilutions over aging over various other
 3 things.
 4 Q. Gotcha. Here in the last
 5 sentence to Ms. Staub's e-mail, she has, "Any
 6 downsides to this...other than the obvious?"
 7 Do you see that? Do you understand what she
 8 meant as to what the obvious downsides were?
 9 MR. SANGIAMO: Objection. Calls
 10 for speculation.
 11 THE WITNESS: I have no -- I
 12 have no idea what Joan thought at that
 13 time.
 14 BY MR. KELLER:
 15 Q. Okay. Do you recall --
 16 A. It's not obvious to me.
 17 Q. -- understanding what the
 18 obvious downsides would be of running an end
 19 expiry study of mumps?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: The first thing it
 23 cost money. The second one would be
 24 that you might not meet the criteria
 25 of the study and then you would have

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 2 to figure out what to do.
 3 BY MR. KELLER:
 4 Q. When you say not meet the
 5 criteria of the study, end up with a
 6 seroconversion rate lower than what was in the
 7 label?
 8 A. No. It could be all kinds of
 9 things. I mean studies, clinical studies
 10 have their problems. You could not have
 11 enough participants or valid assay points to
 12 make any statement.
 13 Q. Sure. If you look on page 2,
 14 there's an e-mail on the 27th of June, 1997
 15 from a Joline Fontaine to you, Dr. Schodel.
 16 Do you see that?
 17 A. Uh-huh. Which one is this?
 18 This here. Where is it?
 19 Q. It's on --
 20 A. She said, "what do you think of
 21 the studies proposed below?"
 22 Q. Correct. Who is Joline
 23 Fontaine?
 24 A. I'm not 100 percent sure, but
 25 she may have been another Merck employee. I

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 2 do remember the name, but what her exact
 3 function was, I don't remember.
 4 Q. Sure. In here you -- in the
 5 e-mail that came after that where you
 6 responded on June 30, 1997, you say here, Dear
 7 Joline, If we decide to address the at expiry
 8 mumps titer versus immunogenicity issues by
 9 clinical trials, I think we should A, not
 10 compare to at release for the obvious risks;
 11 and B, not titrate the virus, because that
 12 risks to change the ratio of mumps and measles
 13 and rubella with possible ensuing changes in
 14 interference.
 15 Do you see that?
 16 A. Uh-huh.
 17 Q. What were you talking about? Do
 18 you recall writing this e-mail?
 19 MR. SANGIAMO: Mr. Keller, I'll
 20 just ask you to let him read the rest
 21 of that e-mail if he has not read it
 22 already.
 23 MR. KELLER: We'll get there.
 24 I'm just asking if he recalls writing
 25 this e-mail.

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2 MR. SANGIAMO: The question is,

3 do you recall writing the e-mail?

4 THE WITNESS: I don't, but I can

5 certainly recall if I reread this

6 again my kind of argumentation here.

7 BY MR. KELLER:

8 Q. Sure. Take whatever time you

9 need. Let me ask you the question, then you

10 can see if you can answer it, if you have to

11 reread it.

12 What did you mean when you

13 decided to address that expiry mumps titers

14 versus immunogenicity issue?

15 MR. SANGIAMO: You should read

16 the remainder of the e-mail.

17 BY MR. KELLER:

18 Q. Or is that versus or is that as?

19 It's confusing to me.

20 A. So there are two -- there are

21 at least two issues in trying to post hoc

22 determine an end expiry titer. Some are

23 linked to the -- well, it's at least three.

24 Some are linked to the general risk of

25 running clinical trials and some are linked

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2 to the -- to what you compare it to. And

3 obviously many vaccines, if you compare them

4 at the high titer, they have -- initially,

5 will have a higher immunogenicity at release

6 which I'm not sure is actually true for

7 mumps. I don't think it is. But for

8 varicella, for example, it's very well known.

9 So if you compare, if you compare the

10 release, the release titers and they're very

11 high to the end expiry titers which are

12 lower, you will see a difference which is

13 fine, but it's a real difference.

14 The second one is how do you

15 actually prepare such a material. And the

16 third one is how do you measure it. And that

17 goes both for the product side and for the

18 clinical side. So in the preparation, we've

19 always made MMR pretty much the same way.

20 It's the same kind of cell culture, it's the

21 same kind of harvest site, it's the same way

22 of blending the viruses. Those viruses are

23 not innocuous to each other. They do stuff

24 to each other when you mix them. We

25 certainly found that out when we did ProQuad.

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2 There's a lot of publications on that.

3 So if you were to hold

4 everything the same but change one of the

5 components, you actually change the whole.

6 So you're no longer comparing the same

7 vaccine. It's not a good way of determining

8 the end expiry. So that's one of the

9 factors.

10 Let me think about what the

11 other factors were. The other factor is the

12 uncertainty of actually knowing exactly what

13 titer of what you have in there because every

14 release assay has variability. And I

15 remember one thing that when this was finally

16 done, which I was not part of, the -- Merck

17 put in a heroic effort to actually determine

18 the exact titers of the mumps component in

19 the MMR that it had specifically created for

20 the trial to compare, as you said before, the

21 medium dose and lower dose to the normal

22 release dose. That was very important

23 because if you just pick a lot that's

24 somewhere sitting in your refrigerator and

25 that had been analyzed, because they analyze

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2 the release assays, happen when the lots are

3 made, so, you know, they may have been

4 analyzed, I don't know, two years ago. The

5 way the assay ran then, you may have a number

6 that is not contemporaneous and it does not

7 reflect the truth of the comparison. Again,

8 we're talking about comparisons. The

9 comparisons is what really matters. So I was

10 also nervous that if you -- in this e-mail,

11 that if you were to construct something like

12 that and not come up with a format of testing

13 that really increased the variability --

14 decreased the variability of the release

15 assays, that not only would you create an

16 artificial situation, you would potentially

17 amplify it by the uncertainty that is

18 inherent in every assay and in every assay

19 depending on the form that it's run.

20 Q. Why wouldn't you want to have an

21 artificial situation?

22 A. Why would I not want to?

23 Because it wouldn't reflect what I put out on

24 the market. And I have been putting out in

25 the market for 40 years. It wouldn't reflect

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 2 the safety, effectiveness and efficacy record
 3 of the vaccine. It would be something
 4 completely contrived.
 5 Q. So you wanted to make sure when
 6 you -- when they were -- if you were going to
 7 do this end expiry study with different
 8 potencies, that the potencies that you were
 9 testing with were as accurate as possible to
 10 that potency that --
 11 A. On one hand as accurate as
 12 possible and on the other hand reflecting the
 13 material that's actually out there on the
 14 market, not something that is just made up in
 15 the lab and then put into people.
 16 Q. Gotcha. So in this e-mail you
 17 talk about the obvious risk, is that the
 18 obvious risk you were talking about?
 19 A. Yeah.
 20 Q. Was there a concern that the
 21 results, if you ran this assay, would be lower
 22 than what was identified in the label?
 23 A. No. This was not -- I'm not
 24 dealing with the label here. I'm just
 25 dealing with comparisons. So there was no

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 2 concern about the label. The concern was
 3 simply that this would not reflect the
 4 situation that we wanted to test.
 5 Q. Here you write, The trial should
 6 only compare seroconversion rates to
 7 acceptable historical seroconversion data
 8 after immunization with lots at expiry, thus
 9 making sure that even lower titers meet the
 10 standards (the problem here is whether the
 11 assays our lab are willing to run are
 12 generally accepted by the agencies or the
 13 scientific public at large, short of
 14 publications I have my doubts).
 15 What assays were you talking
 16 about?
 17 A. Well, so that's the first set
 18 of assays on the product which to make sure
 19 that they're accurately reflecting what's on
 20 the product. Then the other one is that the
 21 assays that are -- whether that's the ELISA
 22 or the PRN, that are currently run are up to
 23 snuff by the standards of when this happened.
 24 Not assays that were run in 1970 or 1965 when
 25 Maurice did his original licensure of MMR.

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 2 So what I was thinking of is simply the
 3 impact of time on regulatory expectations. I
 4 mean, we have a lot of -- these are old
 5 products, they've been extremely successful
 6 in the market. They've been very safe,
 7 they've been given to hundreds of millions of
 8 people and they've worked. We have a low,
 9 very, very low burden of disease in this
 10 country because we use this, different to
 11 almost everywhere else in the world. So the
 12 last thing you want to do is now store it. A
 13 set of comparisons with such a record and
 14 distract from that record by running
 15 something which is not ideally controlled and
 16 very different from what was done in
 17 1960-something. However, standards have
 18 evolved. That was the reference here to the
 19 regulatory agency. So you have to come up
 20 with something which works.
 21 Q. So the fact that when Maurice
 22 Hilleman did the original studies back in the
 23 1960s, there's a expectation, at least a
 24 regulatory expectation, that current modern
 25 assays would be used for these types of tests.

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 2 Correct?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 THE WITNESS: Yes, of course,
 6 but -- they were modern, but, you
 7 know, I was modern in 1956.
 8 BY MR. KELLER:
 9 Q. So in 1997, modern for 1997.
 10 Correct?
 11 A. Yeah.
 12 MR. SANGIAMO: Jeff, we've been
 13 going about an hour and ten minutes.
 14 Are you at or close to a breaking
 15 point?
 16 MR. KELLER: Let me just finish
 17 this document and then we can move on
 18 from there.
 19 BY MR. KELLER:
 20 Q. This concern you talked about
 21 here, the changes in interference, was there
 22 interference with the ratio of virus in the
 23 MMR II vaccine between the different antigens?
 24 MR. SANGIAMO: Object to the
 25 form.

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 2 THE WITNESS: I don't know. I
 3 was -- there was a theoretical
 4 concern.
 5 BY MR. KELLER:
 6 Q. Have you ever seen any
 7 documentation that talks about -- let me
 8 strike that.
 9 When you were working on the
 10 ProQuad licensing applications, did -- was
 11 there any discussion about interference
 12 between the mumps, rubella and measles
 13 antigens in the ProQuad?
 14 A. No, varicella.
 15 Q. It was varicella?
 16 A. Yes. So that, of course -- and
 17 that's published that that interference had
 18 led to the very long half towards ProQuad
 19 licensure because the viruses had to be
 20 appropriately re-titrated. It didn't change
 21 the MMR component but it did change the
 22 varicella component.
 23 Q. Do you recall any discussion at
 24 Merck that there's interference between
 25 measles and higher the amount of measles

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 2 that's added in a dose, the lower the potency
 3 of the mumps?
 4 A. No, I do not. As I said, the
 5 example I just gave you is the ProQuad
 6 example, that one I knew about, but not what
 7 you're saying.
 8 Q. You weren't aware of that?
 9 A. No. Or at least I don't
 10 remember it.
 11 Q. If you look on the next e-mail
 12 from Keith Chirgwin to you and Ms. Fontaine,
 13 who is Keith Chirgwin?
 14 A. Keith Chirgwin was in the
 15 regulatory group. I don't know what his role
 16 was at that time, but he eventually basically
 17 succeeded Henrietta Ukwu and became the head
 18 of vaccine regulatory.
 19 Q. If you see in the middle of
 20 Mr. Chirgwin's e-mail --
 21 A. Which one is that, on the first
 22 page?
 23 Q. 1468951 on the first page.
 24 A. Okay. Okay.
 25 Q. Dated June 30, 1997, at

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 2 6:39 p.m. Mr. Chirgwin writes --
 3 A. Where is this? So this is from
 4 me to -- or is this from -- no, this is --
 5 Q. From Keith Chirgwin. You got
 6 it. To you and Ms. Fontaine. Do you see
 7 that, June 30th?
 8 A. This is from me to --
 9 Q. No, from Keith Chirgwin to you.
 10 A. There's something wrong.
 11 MR. SANGIAMO: It says from.
 12 BY MR. KELLER:
 13 Q. From Keith Chirgwin. I'll go
 14 through that in a second. It's a weird
 15 e-mail.
 16 A. There's something wrong here
 17 because this is a message I sent to Keith
 18 obviously from the text.
 19 Q. Right.
 20 A. But --
 21 Q. Looks like he's cutting and
 22 pasting into his e-mail.
 23 A. Maybe he wrote it and just -- I
 24 don't know. I'll have to read it and see.
 25 Q. It looks like Mr. Chirgwin had

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 2 taken something that you had written
 3 previously, though it's not in any e-mails
 4 that we've been able to find, and then
 5 responded below that. I was wondering if you
 6 look at the part that's attributed to you,
 7 Dr. Schodel, do you recall writing this
 8 particular section?
 9 A. I have certainly not written
 10 this. This is not something I would write.
 11 It's just not my style of writing and I don't
 12 remember this. So this is something that he
 13 pasted in there. In my --
 14 Q. In here it appears that either
 15 he wrote it or where he got this information,
 16 he says -- this e-mail says, What worries me
 17 is there is no clearly defined standards and
 18 we may be waking sleeping dogs up as they say
 19 (especially since I get no clear picture of
 20 whether our assays are generally acceptable.
 21 I get a wide spectrum of answers to the
 22 acceptability of ELISAs only).
 23 Do you see that?
 24 A. Yes.
 25 Q. Do you recall there being a

<p style="text-align: right;">Page 150</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 discussion with respect to doing an end expiry</p> <p>3 study in this time frame, that Merck wanted to</p> <p>4 use just an ELISA assay for its end expiry</p> <p>5 study?</p> <p>6 A. I don't remember that. I don't</p> <p>7 think I've written that, so -- but on the</p> <p>8 other hand, I -- it's a reasonable question</p> <p>9 as to whether the ELISA alone would be</p> <p>10 acceptable and reasonable. That question --</p> <p>11 Q. Why would that be a reasonable --</p> <p>12 A. Well, the ELISA is a much</p> <p>13 better controlled assay than the PRN. By its</p> <p>14 nature it can be. So it's just a more</p> <p>15 reliable assay.</p> <p>16 Q. So the -- here the opposite is</p> <p>17 the concern is that whether the acceptability</p> <p>18 of ELISA alone versus some other assay. So</p> <p>19 why would that --</p> <p>20 A. Well, there was a --</p> <p>21 MR. SANGIAMO: Object to the</p> <p>22 form. Actually, Jeff, did you finish</p> <p>23 your question? You said so here the</p> <p>24 opposite is the concern is that</p> <p>25 whether in the acceptability of ELISA</p>	<p style="text-align: right;">Page 152</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 is or is not acceptable to regulatory</p> <p>3 agencies. By that time there was</p> <p>4 still a strong desire by at least the</p> <p>5 FDA to see virus neutralizing titers,</p> <p>6 functional assay titers for this</p> <p>7 particular virus. That is not -- and</p> <p>8 so they are not opposites. I mean,</p> <p>9 the -- it does not mean that the ELISA</p> <p>10 is not more reliable and better</p> <p>11 standardized. It is simply that the</p> <p>12 expectations may have been different</p> <p>13 at that time.</p> <p>14 BY MR. KELLER:</p> <p>15 Q. Well, an ELISA assay only counts</p> <p>16 antibodies. Correct?</p> <p>17 A. Yes, it does.</p> <p>18 Q. It doesn't count whether or not</p> <p>19 those antibodies protect the kid from getting</p> <p>20 sick?</p> <p>21 MR. SANGIAMO: You have to let</p> <p>22 him finish his answers. He didn't</p> <p>23 just now.</p> <p>24 THE WITNESS: But it does detect</p> <p>25 antibodies reliably.</p>
<p style="text-align: right;">Page 151</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 alone --</p> <p>3 MR. KELLER: I'll rephrase it.</p> <p>4 Let me strike it.</p> <p>5 MR. SANGIAMO: Thank you.</p> <p>6 BY MR. KELLER:</p> <p>7 Q. From the wording of this e-mail</p> <p>8 it appears to me the opposite, that there was</p> <p>9 a concern that there wouldn't be an acceptance</p> <p>10 to the use of ELISA alone, and I'm asking you</p> <p>11 whether or not -- what you understand that to</p> <p>12 mean?</p> <p>13 A. So those are not opposites.</p> <p>14 MR. SANGIAMO: Object. I'm</p> <p>15 sorry, Doctor. Objection. You're</p> <p>16 asking what the author meant, or are</p> <p>17 you asking his interpretation of those</p> <p>18 words?</p> <p>19 MR. KELLER: His interpretation,</p> <p>20 yes.</p> <p>21 MR. SANGIAMO: His interpretation.</p> <p>22 THE WITNESS: So let's first</p> <p>23 talk about acceptability. Acceptability</p> <p>24 would mean acceptability to regulatory</p> <p>25 agencies. I can't speculate on what</p>	<p style="text-align: right;">Page 153</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 MR. KELLER: Let's take a break.</p> <p>3 VIDEOGRAPHER: Off the record at</p> <p>4 11:41. This will end disc number two.</p> <p>5 - - -</p> <p>6 (A recess was taken.)</p> <p>7 - - -</p> <p>8 VIDEOGRAPHER: Back on the</p> <p>9 record 11:55. Beginning of disc</p> <p>10 number three.</p> <p>11 MR. KELLER: For the record I'd</p> <p>12 like to mark as Exhibit 5 a document.</p> <p>13 - - -</p> <p>14 (Exhibit Schodel-5, 2/23/01</p> <p>15 E-mail with attachment, Bates</p> <p>16 MRK-KRA00549510 - 00549535, was marked</p> <p>17 for identification.)</p> <p>18 - - -</p> <p>19 MR. KELLER: For the record,</p> <p>20 Exhibit 5 is a document that bears</p> <p>21 Bates stamp number KRA 549510 through</p> <p>22 535. There is some documents in the</p> <p>23 middle that aren't Bates numbered but</p> <p>24 they are Bates numbered in the way</p> <p>25 they are produced to us, we just</p>

<p style="text-align: right;">Page 154</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 couldn't print them out with Bates</p> <p>3 numbers. So 549518 -- oh, I wasn't</p> <p>4 able to do it. Which is just the</p> <p>5 attachments to this e-mail. So I will</p> <p>6 represent to you they are Bates</p> <p>7 numbered in there. Are there Bates</p> <p>8 numbers in yours?</p> <p>9 MS. ZINSER: Yes.</p> <p>10 MR. KELLER: Good, good, good.</p> <p>11 Strike my last statement.</p> <p>12 BY MR. KELLER:</p> <p>13 Q. Exhibit 5 is a document that</p> <p>14 bears Bates numbers KRA 549510 through 535.</p> <p>15 And I will ask you, Dr. Schodel, you are</p> <p>16 identified as receiving this document and its</p> <p>17 attachments on February 26, 2001, from Dorothy</p> <p>18 Margolskee. I'll ask you, do you recall</p> <p>19 receiving this e-mail and the attachments?</p> <p>20 A. No, but I probably received it</p> <p>21 if it says so.</p> <p>22 Q. Do you have any reason to</p> <p>23 believe that you didn't receive it?</p> <p>24 A. No.</p> <p>25 Q. Do you have any reason to</p>	<p style="text-align: right;">Page 156</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 A. Uh-huh.</p> <p>3 Q. Who is that?</p> <p>4 A. Doug at the time was the head</p> <p>5 of clinical.</p> <p>6 Q. Clinical?</p> <p>7 A. Yeah.</p> <p>8 Q. Clinical research?</p> <p>9 A. Clinical research within MRL.</p> <p>10 So he was reporting to Ed.</p> <p>11 Q. And was it typical to send</p> <p>12 e-mails to Ed Skolnick during this time frame,</p> <p>13 once the information was important?</p> <p>14 MR. SANGIAMO: Object to the</p> <p>15 form. Calls for speculation.</p> <p>16 THE WITNESS: I'd have to</p> <p>17 speculate. Of course. I mean, he was</p> <p>18 somebody who took a lot of interest in</p> <p>19 details.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. And here it was cc'd to Jerry</p> <p>22 Sadoff, Henrietta Ukwu, Emilio Emini, Keith</p> <p>23 Chirgwin, Michael DeAngelo -- Michael Angelo</p> <p>24 and Michael King. Who is Emilio Emini?</p> <p>25 A. Emilio Emini was the head of</p>
<p style="text-align: right;">Page 155</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 believe that you didn't review the attachments?</p> <p>3 A. No. I think I probably read</p> <p>4 them.</p> <p>5 Q. In the attaching e-mails from</p> <p>6 Dorothy Margolskee -- who is Dorothy</p> <p>7 Margolskee during this time frame, what was</p> <p>8 her position?</p> <p>9 A. Dorothy was still my boss at</p> <p>10 the time. She -- I can't tell you what her</p> <p>11 exact title was but she had essentially all</p> <p>12 of vaccine development on the MRL side under</p> <p>13 her.</p> <p>14 Q. Was she on the manufacturing</p> <p>15 side or the laboratory side?</p> <p>16 A. The laboratory side.</p> <p>17 Q. This e-mail on February 23,</p> <p>18 2001, was sent to an Edward Skolnick. Who is</p> <p>19 Edward Skolnick in this time frame?</p> <p>20 A. Ed Skolnick was the head of</p> <p>21 MRL.</p> <p>22 Q. Was he the president of MRL?</p> <p>23 A. Yes.</p> <p>24 Q. Also cc'd -- do you know who</p> <p>25 Douglas Greene was?</p>	<p style="text-align: right;">Page 157</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 the basic research group.</p> <p>3 Q. Was his group --</p> <p>4 A. In MRL.</p> <p>5 Q. -- the one running Protocol 007?</p> <p>6 A. No, his group was the one that</p> <p>7 was running the neutralization assay.</p> <p>8 Q. So his group was --</p> <p>9 A. And possibly the ELISA as well.</p> <p>10 Pretty certain the ELISA as well.</p> <p>11 Q. So his team was the one actually</p> <p>12 running the assays that were part of Protocol</p> <p>13 007?</p> <p>14 A. Not the assays on the protocol</p> <p>15 side -- on the product side, but the assays</p> <p>16 on the clinical side.</p> <p>17 Q. Correct. For part of Protocol</p> <p>18 007, they were doing the PRN assay testing.</p> <p>19 Correct?</p> <p>20 A. Yes.</p> <p>21 Q. They were doing the ELISA</p> <p>22 testing as well?</p> <p>23 A. Yes.</p> <p>24 Q. So it was running in the labs</p> <p>25 that he controlled?</p>

40 (Pages 154 - 157)

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Yes.
 3 Q. Who is Michael Angelo?
 4 A. Michael Angelo was in
 5 manufacturing. I don't know what his exact
 6 role was, but I think quality.
 7 Q. What about Michael King?
 8 A. Also manufacturing.
 9 Q. In the first paragraph,
 10 Ms. Margolskee writes to Mr. Skolnick, "We
 11 have been assisting MMD in responding to CBER
 12 questions re mumps end-expiry by performing an
 13 interim analysis on 600 children participating
 14 in the mumps end-expiry study (200 per groups,
 15 studied at mumps potencies of 4.9, 4.0 and
 16 3.7)."
 17 Do you see that?
 18 A. Yes.
 19 Q. Do you recall Merck conducting a
 20 preliminary subset analysis of Protocol 007's
 21 PRN assay?
 22 A. Yes.
 23 Q. Do you know why it ran that
 24 assay -- did a preliminary look at the
 25 results?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. I'm not sure, but it may have
 3 been due to CBER questions.
 4 Q. Was it common to unblind a study
 5 in the middle of it to take a look at the
 6 results of a subset?
 7 A. This is making an assumption.
 8 I don't know how much unblinding was done.
 9 Unblinding had all kinds of different levels
 10 of detail.
 11 Q. Why --
 12 A. Interim analysis would be run
 13 based on the data then available. And it
 14 could be done in a blinded or in an unblinded
 15 fashion. And it could be group unblinded or
 16 individual unblinded. So there's all kinds
 17 of details. I don't know what the details
 18 are here.
 19 Q. Do you -- why are assays
 20 blinded -- strike that.
 21 Why would a plaque reduction
 22 neutralization assay be blinded?
 23 MR. SANGIAMO: Object to form.
 24 THE WITNESS: Every assay would
 25 be blinded in the lab to make sure

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 that the lab doesn't know what group
 3 it belongs to to avoid any potential
 4 bias.
 5 BY MR. KELLER:
 6 Q. And --
 7 A. You're -- I mean, are you
 8 assuming that the lab was unblinded to the
 9 individual assays? There's nothing would
 10 suggest that.
 11 Q. So it's your testimony that when
 12 the preliminary subset analysis was run, that
 13 the lab was not unblinded to the results of
 14 that assay?
 15 MR. SANGIAMO: Objection.
 16 THE WITNESS: What do you mean
 17 with unblinding? I mean, unblinding
 18 would -- so the lab was, of course,
 19 not blinded to the results of the
 20 assays they run because they run the
 21 assay and they report the data. But
 22 they would not know who the sera comes
 23 from. So that's the important part.
 24 They wouldn't know whether it comes
 25 from one group or the other group as

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 well. And the analysis is done by
 3 statisticians so it's not the lab who
 4 does the analysis.
 5 BY MR. KELLER:
 6 Q. You said the reason that you
 7 would do blinding was to protect against bias.
 8 Correct?
 9 A. Right.
 10 Q. And so you said that for the
 11 plaque reduction neutralization assay it was
 12 important to blind the folks doing the assays
 13 as to the different potency groups. Correct?
 14 MR. SANGIAMO: Objection.
 15 THE WITNESS: Yeah.
 16 MR. SANGIAMO: Are you asking
 17 him about -- questions about decisions
 18 that were made about Protocol 007 and
 19 the running of the assay in Protocol
 20 007 --
 21 MR. KELLER: I'm asking
 22 questions about --
 23 MR. SANGIAMO: -- or are you
 24 asking in general -- let me finish my
 25 question. Are you asking for general

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 expert testimony or are you asking
 3 for --
 4 MR. KELLER: Dino, you can
 5 object and that's it. Speaking
 6 commentaries are not appropriate.
 7 MR. SANGIAMO: Well, I've let
 8 you go a long time with these
 9 hypothetical questions. I think at a
 10 minimum you need to clarify for the
 11 witness --
 12 MR. KELLER: Instruct the
 13 witness not to answer then. Stay out
 14 of my deposition, Dino.
 15 MR. SANGIAMO: I think you need
 16 to make it clear what you're asking.
 17 BY MR. KELLER:
 18 Q. Dr. Schodel, are you aware of
 19 how Protocol 007 was blinded?
 20 A. No.
 21 Q. For plaque reduction neutralization
 22 assay would you expect, based on your 30 years
 23 of experience and participating with these
 24 protocols, that the groups of -- the three
 25 different potencies would have been blinded to

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 the people doing the assays?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 THE WITNESS: Like any other
 6 assay that goes into the lab that
 7 would be blinded. Priority blinded
 8 studies are generally given blinded
 9 into the lab.
 10 BY MR. KELLER:
 11 Q. Would you have expected there to
 12 be blinding as to whether or not it was a pre
 13 or postvaccination sample?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: Not necessarily.
 17 Because of the timing as to when the
 18 assays are run. If they're run
 19 parallelized, they may have been
 20 blinded. If they're run as they come
 21 in, they would not have been blinded
 22 because they come in at a certain
 23 time, not perfectly blinded, but they
 24 still would not specify that.
 25 BY MR. KELLER:

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. What are the benefits of
 3 blinding the prevaccination versus the
 4 postvaccination --
 5 MR. SANGIAMO: Object to the
 6 form.
 7 BY MR. KELLER:
 8 Q. -- based only your experience?
 9 MR. SANGIAMO: Object to form.
 10 THE WITNESS: I'm not sure there
 11 are any.
 12 BY MR. KELLER:
 13 Q. Somebody running the assays for
 14 a plaque reduction neutralization, the
 15 prevaccination serum you'd expect to see a
 16 whole lot of plaque in those samples. Correct?
 17 A. Yes, that's correct.
 18 Q. And in the postvaccination group
 19 you would expect to see fewer plaques. Correct?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: That's correct.
 23 BY MR. KELLER:
 24 Q. So if the person counting the
 25 assays or counting the plaques to determine

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 how many are in each of those dishes, if they
 3 know it's a prevaccination versus a
 4 postvaccination, that could introduce bias
 5 into their counting, couldn't it?
 6 MR. SANGIAMO: Object to the
 7 form.
 8 THE WITNESS: Depends on how
 9 it's otherwise controlled.
 10 BY MR. KELLER:
 11 Q. How else could it be otherwise
 12 controlled to prevent bias?
 13 A. By an SOP.
 14 Q. So how would an SOP prevent bias
 15 if the person counting the plaques know which
 16 ones are the prevaccination serum and which
 17 are postvaccination?
 18 A. They don't know.
 19 MR. SANGIAMO: Object to the
 20 form.
 21 THE WITNESS: They don't know
 22 that. They can only speculate on it
 23 because they're not told that this is
 24 pre or postvaccination. They wouldn't
 25 know, for example, whether it's a

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 postvaccination sample with a low
 3 titer or a prevaccination titer --
 4 prevaccination sample with a high
 5 titer, which also exists. So they
 6 simply wouldn't know.
 7 BY MR. KELLER:
 8 Q. Is that from your personal
 9 knowledge or are you just -- or is that a
 10 general statement?
 11 MR. SANGIAMO: Object to the
 12 form.
 13 THE WITNESS: I don't know
 14 exactly what the lab did in this
 15 particular case, but it's --
 16 BY MR. KELLER:
 17 Q. If the folks running the lab
 18 were -- knew which samples were prevaccination
 19 serum and postvaccination serum and were
 20 running whether or not they were
 21 seroconverting as the assay was going on,
 22 would that cause you concern from a bias
 23 standpoint?
 24 MR. SANGIAMO: Objection.
 25 THE WITNESS: That's making too

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 many assumptions. They don't
 3 generally know and I don't see the
 4 interest they would have in the lab to
 5 have any impact on that. I mean, all
 6 they do is count holes and record
 7 them. And they have to -- actually
 8 the plates that are counted are kept.
 9 So if they were to count wrong, yet
 10 another control because you can go
 11 back and count again.
 12 BY MR. KELLER:
 13 Q. That's the reason why you count
 14 the plates, so that they could be used as a
 15 quality control?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: In principle.
 19 BY MR. KELLER:
 20 Q. Are you aware of --
 21 A. Or take a photograph.
 22 Q. Are you aware of anybody
 23 destroying the plates in Protocol 007 before
 24 the assays were completed?
 25 A. I was never in the lab neither

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 physically nor -- I have no idea about these
 3 things.
 4 Q. Do you know who David Krah is?
 5 A. Yes, I know David.
 6 Q. What is your opinion of David
 7 Krah?
 8 MR. SANGIAMO: Mr. Keller,
 9 you're not letting him finish his
 10 answers.
 11 THE WITNESS: Highly qualified
 12 scientist, very personable.
 13 BY MR. KELLER:
 14 Q. Did you ever hear of anybody
 15 calling him a fraud?
 16 A. No.
 17 Q. Did you hear anybody stating
 18 that he committed fraud in a clinical study?
 19 A. No.
 20 Q. That would surprise you?
 21 A. Yes.
 22 Q. Did you ever see the preliminary
 23 results from Protocol 007, this interim
 24 analysis of 600 kids?
 25 A. Well, according to the e-mail I

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 did. I'd have to say that I didn't -- it was
 3 not in the front of my mind for the last --
 4 Q. Gotcha. So let me direct your
 5 attention --
 6 A. -- almost 20 years.
 7 Q. -- to 549517.
 8 MR. SANGIAMO: Jeff, you got to
 9 let him finish. You know you're doing
 10 it. You got to let him finish.
 11 THE WITNESS: It's okay.
 12 MR. SANGIAMO: She got it. She
 13 got the additional testimony.
 14 BY MR. KELLER:
 15 Q. So let me direct your attention
 16 to 549517.
 17 A. 549517.
 18 Q. Do you see that?
 19 A. Okay.
 20 Q. And are these the preliminary
 21 results of Protocol 007 of those 600 kids?
 22 MR. SANGIAMO: Objection.
 23 Answer if you know, Dr. Schodel.
 24 THE WITNESS: What it says here
 25 is that they are the draft results of

<p style="text-align: right;">Page 170</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 the preliminary subset analysis.</p> <p>3 BY MR. KELLER:</p> <p>4 Q. Here under the topic it says,</p> <p>5 Jon Hartzel biometrician vaccine, do you know</p> <p>6 who Jon Hartzel is?</p> <p>7 A. Yes, I do.</p> <p>8 Q. Is it your understanding that</p> <p>9 Mr. Hartzel is the one that ran this analysis?</p> <p>10 A. The statistical analysis, yes.</p> <p>11 Q. And who did Mr. Hartzel work for</p> <p>12 at Merck Research Labs during this time frame?</p> <p>13 A. He works for Merck Research</p> <p>14 Labs.</p> <p>15 Q. Do you know who he reported to?</p> <p>16 A. Probably -- I don't really</p> <p>17 know. Probably Joe Heyse.</p> <p>18 Q. And do you know who Joe Heyse</p> <p>19 reported to?</p> <p>20 A. Ultimately Doug Greene, I</p> <p>21 think. But, again, I'm not sure. So the</p> <p>22 better answer would be I don't know.</p> <p>23 Q. Let me direct your attention to</p> <p>24 page 549519, and tell me if you --</p> <p>25 A. 549 --</p>	<p style="text-align: right;">Page 172</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 do you want to know?</p> <p>3 BY MR. KELLER:</p> <p>4 Q. What does this document represent</p> <p>5 to you? What is it reporting?</p> <p>6 A. It looks like a table.</p> <p>7 Q. Is it reporting by potency group</p> <p>8 4.9, 4.0 and 3.7 for each of the subjects</p> <p>9 identifying the titers and whether or not they</p> <p>10 seroconverted for the preliminary subset</p> <p>11 analysis of Protocol 007?</p> <p>12 A. I don't see the grouping here.</p> <p>13 What I do see is serostatus attributions. It</p> <p>14 has the report. It has that here.</p> <p>15 Q. So this is the unblinded results</p> <p>16 of the preliminary subset analysis. Is that</p> <p>17 correct?</p> <p>18 A. It's at least partly unblinded.</p> <p>19 It's unblinded by group allocation.</p> <p>20 Q. And it identifies each kid that</p> <p>21 was tested by their titers and whether or not</p> <p>22 they seroconverted. Correct?</p> <p>23 MR. SANGIAMO: Objection.</p> <p>24 Answer if you know.</p> <p>25 THE WITNESS: It doesn't</p>
<p style="text-align: right;">Page 171</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 Q. 519. This is a group of</p> <p>3 documents --</p> <p>4 A. 518 here.</p> <p>5 Q. -- through 535 entitled, "MMRII</p> <p>6 007 Subset Analysis PRN Assay Listing for</p> <p>7 Subjects Initially Seronegative."</p> <p>8 Do you see that?</p> <p>9 A. No. Okay. Here we go.</p> <p>10 Q. What do you understand this</p> <p>11 document to be?</p> <p>12 MR. SANGIAMO: For the record, I</p> <p>13 don't think Dr. Schodel has been given</p> <p>14 the chance to read the cover e-mail.</p> <p>15 So I want that noted before he answers</p> <p>16 the question.</p> <p>17 BY MR. KELLER:</p> <p>18 Q. This was attached to the e-mail</p> <p>19 that you receive. Correct?</p> <p>20 MR. SANGIAMO: In 2001.</p> <p>21 THE WITNESS: In 2001 and it has</p> <p>22 a lot of pages. So let me at least</p> <p>23 get to the page before I tell you</p> <p>24 whether it tells anything to me other</p> <p>25 than that you told me a page. So what</p>	<p style="text-align: right;">Page 173</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 identify them. It just lists their</p> <p>3 values in a row. That's different</p> <p>4 from identifying them because it</p> <p>5 doesn't give an identifier to which</p> <p>6 kid that might be.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. Right. It identifies the</p> <p>9 results for those approximately 600 kids.</p> <p>10 Correct?</p> <p>11 A. As far as I can tell, it</p> <p>12 identifies the results in these two assays</p> <p>13 here.</p> <p>14 Q. And it identifies the</p> <p>15 prevaccination titer and the postvaccination</p> <p>16 titer. Correct?</p> <p>17 A. Yes, that's true.</p> <p>18 Q. It also identified whether or</p> <p>19 not the child seroconverted. Correct?</p> <p>20 A. I assume so because it says</p> <p>21 sero is probably not in one, but I have to</p> <p>22 speculate because it doesn't say that here.</p> <p>23 Q. Do you know whether or not these</p> <p>24 documents -- these documents are also provided</p> <p>25 to Dr. -- to Ed Skolnick as well as part of</p>

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 this e-mail?
 3 A. They would appear to have been
 4 because unless something else was attached to
 5 the e-mail sent to me.
 6 Q. So this was also provided to
 7 Emilio Emini who was head of the lab that was
 8 running the PRN assay?
 9 A. That's correct.
 10 Q. If you go to the first page of
 11 the e-mail that was sent to Mr. Skolnick and
 12 forwarded on to you, Doctor, Emilio goes on
 13 and says, On the basis of this analysis and
 14 what is currently calculated by MMD as mump
 15 stability in MMR-II (obtained from analyses of
 16 recent MMD stability lots since the summer of
 17 1998), there are MMD "lots in question" that
 18 have been released in the past 2 years.
 19 Do you see that?
 20 A. Yes.
 21 Q. And so do you know what they're
 22 referring to as this recent stability, MMD
 23 stability, do you recall there being a
 24 stability analysis of these lots since 1998 to
 25 current?

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 2 MR. SANGIAMO: Object to the
 3 form.
 4 THE WITNESS: I don't recall
 5 that one specifically, but there is
 6 always lots on stability.
 7 BY MR. KELLER:
 8 Q. So what is Merck looking at --
 9 when you say lots are on stability, what do
 10 you understand that Merck is looking at with
 11 regard to testing lots on stability?
 12 A. Well, it's -- a part of a
 13 regulated product manufacturing is that you
 14 put a certain sample of lots on stability,
 15 routine stability testing and you determine
 16 whether they maintain stability through shelf
 17 life. The analysis of that which takes into
 18 account the totality of the data will tell
 19 you whether it does or does not meet the
 20 stability criteria.
 21 Q. So here it says, "These lots may
 22 still be in circulation with 24 month
 23 end-expiry...that fall below 3.7 (6 lots) or
 24 between 4.0 and 3.7 (100 others)."
 25 You understand that 3.7 and 4.0

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 2 represent log potency. Correct?
 3 A. Yes.
 4 Q. The less than 3.7 lots are of
 5 particular concern; the 3.7 to 4.0 lots are
 6 likely defensible with some additional work.
 7 106 lots are a compliance issue.
 8 Do you see that?
 9 A. Uh-huh.
 10 Q. Do you recall at this time frame
 11 that the end expiry potency was 4.3 log?
 12 A. No, I don't.
 13 Q. Do you understand what is
 14 understood -- what is meant here by "a
 15 compliance issue"?
 16 A. Well, compliance issue might be
 17 that if Merck had data that the lot did not
 18 meet the then expectations of the FDA in
 19 terms of potency through shelf life, that
 20 lots would have to be recalled.
 21 Q. So do you recall there being a
 22 discussion at Merck during this time frame
 23 about recalling those 106 lots for being below
 24 the end expiry requirement in this letter?
 25 A. I don't recall that. That's

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 2 something you would have to ask the
 3 manufacturing guys. But in all probability
 4 there was a discussion that's referenced here
 5 as whether these lots are -- whether these
 6 are just individual outliers without any
 7 significance or whether they are a reason to
 8 recall.
 9 Q. So if a lot is released below
 10 the end expiry specification, under what
 11 circumstances would regulations, federal
 12 regulators FDA require those lots to be
 13 recalled, if you know --
 14 MR. SANGIAMO: Object to the
 15 form.
 16 BY MR. KELLER:
 17 Q. -- during this time frame?
 18 MR. SANGIAMO: As he said,
 19 answer if you know. And object to
 20 form.
 21 THE WITNESS: Yeah, it's not an
 22 absolute, there's not an absolute
 23 rule. It would depend on an analysis
 24 of -- we're not talking about lots
 25 that are released under specifications.

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 2 They were released under
 3 specifications. And at the time the
 4 end expiry rules were evolving.
 5 Individual time points of the
 6 stability study because of the
 7 variability of the assay can always
 8 fall under specifications. And the
 9 model is a model. There would have to
 10 be additional research being done in
 11 the lab in manufacturing to determine
 12 whether the actual lots were actually
 13 meeting expectations or not, and then
 14 there would have been to be a
 15 discussion as to what, if they weren't
 16 meeting expectations, what that would
 17 mean and whether it would be better
 18 for the vaccinees to go through a
 19 recall and revaccination or whether it
 20 was -- whether there were enough data
 21 to defend the product as it was
 22 released.
 23 BY MR. KELLER:
 24 Q. Was there a -- when an issue
 25 like this would come up where the product

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 2 would be -- do you understand the term "out of
 3 specification"?
 4 A. Yes.
 5 Q. What is that -- what's your
 6 understanding of that term as used at Merck?
 7 MR. SANGIAMO: Object to the
 8 form.
 9 THE WITNESS: Well, it --
 10 MR. SANGIAMO: Object to the
 11 form. You can answer.
 12 THE WITNESS: It in general
 13 means that a product at some point
 14 doesn't meet the expected specifications.
 15 BY MR. KELLER:
 16 Q. That could be the end expiry
 17 specification?
 18 A. If that end expiry
 19 specification is formally set and if it --
 20 yes, then theoretically it could be that.
 21 Q. Have you ever seen the term
 22 "compliance issue" used at Merck before other
 23 than in this document?
 24 A. Yeah. In all pharmaceutical
 25 companies you talk about -- sometimes about

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 2 compliance issues, yes. It's a lose term.
 3 It doesn't mean all that much.
 4 Q. It doesn't mean all that much,
 5 compliance?
 6 A. Well, it means that there is --
 7 that -- obviously compliance means compliance
 8 with all relevant rules and regulations. And
 9 so there's a wide spectrum of things that
 10 compliance issue can mean. It can mean that
 11 you need additional data to figure out
 12 whether you're in compliance with rules and
 13 regulations or it can mean that you've
 14 discovered that something is outside of rules
 15 and regulation and then you act upon it.
 16 Q. Do you know whether or not Merck
 17 ever reported these 106 lots that are
 18 compliance issue to the FDA?
 19 MR. SANGIAMO: Objection. Calls
 20 for speculation.
 21 THE WITNESS: I do not know.
 22 BY MR. KELLER:
 23 Q. If Merck's 106 lots were out of
 24 compliance with the specification, would you
 25 have expected Merck to have disclosed that to

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 the FDA?
 3 MR. SANGIAMO: Objection.
 4 THE WITNESS: I don't know
 5 whether they were out of compliance,
 6 and as I said, I don't know.
 7 BY MR. KELLER:
 8 Q. At the time of Protocol 007 they
 9 were doing testing, they were testing three
 10 different potencies, correct, 4.9, 4.0 and
 11 3.7? Correct?
 12 A. That's correct.
 13 Q. The 4.9 was the dose that
 14 released -- the dose was released to the
 15 market. Correct?
 16 A. That's correct.
 17 Q. And the 4.0 and 3.7 were below
 18 what that current end expiry was that they're
 19 required to comply with. They were trying
 20 to -- back up.
 21 Protocol 007, purpose of
 22 Protocol 007 was to lower the end expiry
 23 dosage that was identified in the label.
 24 Correct?
 25 A. I don't recall -- I don't

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2 recall it with that precision. I think it

3 was a quite substantial effort to establish

4 the data for a scientifically supported end

5 expiry label in the label. With the changes

6 in labeling philosophy, that we have

7 discussed initially when we started this

8 interview.

9 Q. If you look on -- under the

10 "First, the neuts data," neuts, that means,

11 that represents -- is that -- do you

12 understand it to mean the neutralization data

13 from the preliminary subset analysis of

14 Protocol 007?

15 A. Yeah.

16 Q. In the second bullet point it

17 says, "By the neutralization assay, an MMR-II

18 mumps end-expiry of 4.0 meets CBER's demand

19 for a 90% seroconversion rate floor...."

20 Do you see that?

21 A. Yes.

22 Q. Did you understand that CBER was

23 requiring a 90 percent seroconversion rate

24 floor?

25 A. Unfortunately I don't remember

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2 that MMR, but...

3 Q. ...while the 3.7 log titer

4 misses (88.2 percent seroconversion, with 95

5 percent CI of 82.3 to 92.6 percent).

6 Do you see that?

7 A. Yes.

8 Q. CI, that's -- what do you

9 understand CI to represent?

10 A. Confidence interval.

11 Q. 95 percent confidence interval,

12 that was the criteria upon which you -- this

13 document identifies Protocol 007, the criteria

14 that was being required by the FDA?

15 A. Yes.

16 Q. Here it says, (Jerry and I feel

17 3.7 is medically okay and may be defensible to

18 the Office of Compliance; see below). Lots

19 which have 24 months end expiry titers

20 below -- lower than 3.7 lots would not have

21 data from this study to support the

22 shelf-life.

23 Do you see that?

24 A. Yes.

25 Q. What is your understanding with

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2 respect to the statement "medically ok"? What

3 are they looking at here with respect to these

4 106 lots and whether or not they're medically

5 okay? Do you have an understanding?

6 MR. SANGIAMO: Objection. Calls

7 for speculation. I also want to note

8 he's still not given a chance to read

9 this document.

10 THE WITNESS: I really don't

11 know what they meant precisely. It's

12 a pretty loose term. As you know, the

13 compendial specifications in the EU is

14 3.7. It's also pretty clear when you

15 look at the data, that even though the

16 number seems to be lower than the ones

17 for 4.0 and 4.9, it's still a pretty

18 high number of seroconversions. So

19 there's not a reason to assume --

20 since there is not direct correlation

21 between titers and protection, there's

22 no reason to assume that it would be

23 clinically less efficacious.

24 BY MR. KELLER:

25 Q. So then what is the purpose of

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2 having -- doing an analysis of seroconversion

3 if -- let me strike that.

4 So is it your testimony that it

5 may be medically okay for kids who got

6 vaccines that had end expiries below, in this

7 case, 4.0 and because the seroconversion rate

8 was close to the 4.0 and the 4.9?

9 MR. SANGIAMO: Object to the

10 form.

11 THE WITNESS: That was not the

12 totality of my argument but a part of

13 it. I would say that it would still

14 be -- provide a substantial level of

15 protection against all components in

16 the vaccine.

17 BY MR. KELLER:

18 Q. Well, here Merck is -- CBER is

19 demanding a 90 percent seroconversion floor

20 for purposes of Protocol 007. Do you see

21 that?

22 A. That's what I read here, yes.

23 Q. Do you know why FDA set 90

24 percent as a seroconversion floor?

25 A. I can't speculate as to why the

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 2 FDA set 90 percent as an absolute number
 3 floor.
 4 Q. And so just so I back up, is
 5 Merck -- it looks -- it appears to me from
 6 reviewing the parts that we've gone over, that
 7 Merck is using as its defense of whether or
 8 not the lots that have been released at below
 9 4.0 and at 3. -- between 3.7 and 4.0 are
 10 relying upon the data from the preliminary
 11 subset of Protocol 007. Correct?
 12 MR. SANGIAMO: You mean this one
 13 bullet point that I'm reading?
 14 MR. KELLER: Yes.
 15 THE WITNESS: I don't think that
 16 that's the entire argument. And I
 17 don't know the entire argument. What
 18 you see here, to the extent that I
 19 remember this, is an effort to use the
 20 data as data supporting the argument.
 21 But it doesn't mean that that's what
 22 Merck relied on for anything.
 23 BY MR. KELLER:
 24 Q. But it appears that there -- as
 25 at least one data point to determine whether

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 2 or not these lots are medically okay and
 3 defensible with the Office of Compliance --
 4 let me strike that.
 5 The Office of Compliance, that's
 6 the FDA. Correct?
 7 A. I don't know. It's not -- this
 8 is a strange term. I don't really know what
 9 that is. It's probably an office within the
 10 FDA, but I'd have to speculate.
 11 Q. So is it fair to say that at
 12 least for this part of the argument, analysis
 13 for whether or not these lots are medically
 14 okay, Merck is relying upon this preliminary
 15 subset results of Protocol 007?
 16 A. I would not word it that way.
 17 I think Merck is looking at the subset
 18 analysis to provide current data as to how
 19 the vaccines are behaving relative to each
 20 other. It does not entirely rely on anything
 21 in that study to say that the lots are okay,
 22 or not okay for that matter.
 23 Q. I see. And so you say how they
 24 behaved together. So what your -- is it your
 25 position that because in Merck's preliminary

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 2 subset of Protocol 007, the 4.9 dose group had
 3 a seroconversion rate of 94 percent,
 4 94.1 percent and the 3.7 group had a
 5 seroconversion rate of 88.2 percent, and that
 6 those are highly -- or so close in number that
 7 all that matters is how those numbers compare
 8 to each other and not the actual results of
 9 whether or not they -- let me strike that.
 10 That's a terrible question.
 11 How do you understand -- you
 12 testified that they're comparing -- they're
 13 using it to compare how the different groups
 14 performed to justify that these lots released
 15 at end expiry of 3.7 are medically okay. Can
 16 you explain that to me a little more detail?
 17 I'm not sure I understand it.
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: So I would see
 21 this very differently. This is --
 22 testing them in a clinical trial is
 23 more an exercise of willingness to
 24 provide data on a future end expiry
 25 dose that will be written into the

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 2 appropriate manufacturing
 3 documentation. It -- the trial was
 4 not run with the intent of justifying
 5 anything in that regard.
 6 So when you then look at the
 7 data, you see that actually all three
 8 groups provide very respectable
 9 seroconversion rates, and it would
 10 probably be hard to tell them
 11 statistically apart even though they
 12 appear different which often deceives
 13 the eye because you see a number, it
 14 is a different number. But if you
 15 look at the confidence intervals,
 16 they're overlapping. So I'm not sure
 17 that even just looking at this little
 18 fragment, which is not even the
 19 complete study, it's incomplete
 20 numbers, you would be able to tell
 21 them apart. So they're all behaving
 22 fairly well. Which provides
 23 additional information that's relevant
 24 to the question as to whether low
 25 titered -- or lower titered lots might

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 2 be clinically acceptable doesn't mean
 3 that that's what you would use in your
 4 label because you have an excess of
 5 caution, you make sure that you're
 6 always above a certain threshold. But
 7 actually what this provides to me is
 8 reassurance that even a somewhat lower
 9 titered vaccine is still performing
 10 quite well.
 11 BY MR. KELLER:
 12 Q. And in you're relying upon the
 13 seroconversion rate for that?
 14 A. No, I look at the whole thing.
 15 I look at the titers and the seroconversion
 16 rate. And I don't have the ELISA titers in
 17 front of me unfortunately, which are even
 18 more important because the ELISA has less
 19 variability. And I don't have the complete
 20 analysis. So you're talking about an interim
 21 analysis. But in the meantime, the complete
 22 data would be much more helpful to actually
 23 look at the complete data set rather than
 24 just an interim set. That was just what was
 25 known at the time.

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 2 Q. I see. I apologize if I'm a bit
 3 confused. Let me ask you this question: If
 4 here Merck is relying upon the seroconversion
 5 numbers of the preliminary subset as support
 6 and comfort that doses that have an end expiry
 7 of 3.7 would be medically okay when you
 8 testified earlier that the -- Merck never
 9 tested the specificity of its plaque reduction
 10 neutralization assay that you're aware of.
 11 MR. SANGIAMO: Object to the
 12 form. Actually there's no question
 13 yet. Is there a question?
 14 BY MR. KELLER:
 15 Q. My question is, if the
 16 specificity of these plaque reduction
 17 neutralization assays was low, wouldn't that
 18 affect the seroconversion rates that were
 19 reported across all three dosage ranges?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 BY MR. KELLER:
 23 Q. And underestimate seroconversion
 24 -- overestimate -- I'm sorry, overestimate
 25 seroconversion?

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 2 A. I think you gave the answer
 3 into your relatively convoluted question
 4 yourself. I'm not sure I can even follow it
 5 entirely. But the answer was at the end when
 6 you said that they were all similar. That
 7 basically tells you that sensitivity of the
 8 assay is not the major factor in determining
 9 whether these lots are different or not.
 10 Q. Well, the 3.7 that's derived was
 11 derived in a different assay. That was
 12 derived from a potency assay, not a plaque
 13 reduction neutralization assay.
 14 A. Yeah, but when they're put in
 15 people, they behave relatively similar. It
 16 doesn't matter whether I have a number here
 17 of 70 percent seroconversion or 90 percent
 18 seroconversion and a titer that's slightly
 19 lower or higher. I compare the three cells.
 20 And if the confidence intervals overlap, I
 21 tell you I can't tell them apart which means
 22 they're all potent in the clinic. The
 23 absolute numbers don't tell me anything.
 24 Q. So it's your view that
 25 seroconversion is irrelevant for purposes of

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 2 analyzing what happened in Protocol 007 --
 3 A. No.
 4 Q. -- the PRN assay?
 5 A. That's not what I said. And
 6 you're trying to lead me into saying
 7 something which I absolutely did not say. I
 8 did not say that seroconversion was not
 9 important. I said that it is similar between
 10 the groups. It is not important for
 11 predicting efficacy. That's what I said.
 12 MR. SANGIAMO: Jeff, it's 12:32.
 13 MR. KELLER: That's fine.
 14 VIDEOGRAPHER: Off the record at
 15 12:32.
 16 - - -
 17 (A recess was taken.)
 18 - - -
 19 VIDEOGRAPHER: Back on the
 20 record at 1:29.
 21 BY MR. KELLER:
 22 Q. Doctor, can you put Exhibit 5
 23 back in front of you? Let me direct your
 24 attention to 549511. In the middle of the
 25 page it says, "Background/Impact Assessment" --

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2 A. Wait. Wait a second. 5495 --

3 Q. 511.

4 A. Okay.

5 Q. It's the second page of the

6 document.

7 In the middle of the document it

8 says, "Background/Impact Assessment on

9 Marketed Product." Do you see that?

10 A. Uh-huh.

11 Q. In the middle bullet point it

12 says, In the meantime, there has been

13 continuing discussions with CBER re mumps end

14 expiry titers. In response to recent CBER

15 inspection from the Office of Compliance to

16 MMD, manufactured mumps stability data was

17 re-examined. In that analysis, it appears

18 that mumps stability has been somewhat less

19 (i.e. around .2 logs faster over a 24 months

20 period; a total of around 1.0 log lost over

21 24 months) for lots manufactured at least

22 since the summer of 1998.

23 Do you see that?

24 A. Yes.

25 Q. Were you aware that based on

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2 Merck's then current mumps stability models,

3 that it was projecting an approximate 1.0 log

4 loss over the shelf life of its product?

5 MR. SANGIAMO: Object to the

6 form.

7 THE WITNESS: I may have been

8 aware of it. As you know, I didn't

9 work in manufacturing, so this wasn't

10 exactly my line of business.

11 BY MR. KELLER:

12 Q. Do you recall any discussion at

13 Merck regarding the stability models that

14 projected a one log loss over 24 months?

15 A. Not in any detail.

16 Q. What generally do you understand

17 those conversations to take place?

18 MR. SANGIAMO: Objection.

19 THE WITNESS: I was not involved

20 in the modeling exercises so I

21 wouldn't -- it wouldn't have been

22 discussed with me. I mean, what would

23 have been discussed with me is more

24 the interpretation of clinical data.

25 BY MR. KELLER:

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2 Q. Do you recall there being

3 discussions of the 1.0 log loss over 24 months

4 to be at issue with Merck's complying with its

5 end expiry specifications of its label for the

6 mumps component?

7 A. Not that specifically.

8 Q. You just generally recall that?

9 A. I generally recall that when

10 there were data like the ones that are

11 suggested initially of lots on stability not

12 being above a certain titer that there was

13 sometimes a discussion about that. I don't

14 remember any detailed discussion about the

15 modeling piece.

16 Q. Do you recall any discussion

17 about anybody who criticized the model that

18 Merck was using at Merck within Merck's

19 employees that calculated this projected 1.0

20 log loss at 24 months?

21 MR. SANGIAMO: Objection. Form.

22 THE WITNESS: No.

23 BY MR. KELLER:

24 Q. If you go back to the document,

25 the second bullet point it says, "Given this

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2 new analysis, lots manufactured since...1999

3 are still fine with the overfill and 24 month

4 end-expiry titers projected at or above 4.0."

5 Do you see that?

6 A. Yes.

7 Q. Do you recall what they're

8 talking about for the overfill?

9 MR. SANGIAMO: Objection. Calls

10 for speculation.

11 THE WITNESS: I can read this

12 and tell you what an overfill would

13 be, but I'm not sure -- I don't

14 remember the details.

15 BY MR. KELLER:

16 Q. What's your understanding of an

17 overfill?

18 A. Overfill would be that you fill

19 in more vaccine than you have previously at

20 least by that assay.

21 Q. Do you recall that in September

22 of 1999 Merck and CBER -- or CBER required and

23 Merck agreed to overfill its minimum release

24 specification to 5.0?

25 MR. SANGIAMO: Object to the

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 2 form.
 3 THE WITNESS: Not in that detail
 4 but now that -- you know, this makes
 5 sense in the context.
 6 BY MR. KELLER:
 7 Q. So in the last bullet point on
 8 this page it says, Unfortunately, with the
 9 faster mumps potency loss rates seen since at
 10 least summer of 1998, there are released lots
 11 which, at 24 months, are projected to be below
 12 4.0 (100 lots) or 3.7 (6 lots). This will be
 13 a compliance issue with the Agency.
 14 Do you see that?
 15 A. Yes, I see that.
 16 Q. Do you understand that to mean
 17 the agency is the FDA?
 18 A. It could have referred to the
 19 FDA or to other agencies as well.
 20 Q. During this time frame, did you
 21 understand that the -- at this time the label
 22 required that at end expiry there would be 4.3
 23 log?
 24 A. I think this was just -- this
 25 was still in the -- I don't remember exactly

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 2 whether at this time the label was already
 3 defined as an end expiry label as it was
 4 later on understood to be, whether it was a
 5 release label essentially.
 6 Q. Do you remember at some point
 7 the end expiry log being set at 4.3?
 8 A. I'm not -- I'm a bit murky on
 9 the details here. It probably was, but
 10 I'm --
 11 Q. If -- when this says -- when
 12 this e-mail that was sent to the president of
 13 Merck in February of 2001 says this will be a
 14 compliance issue with the agency, who at Merck
 15 would decide whether or not to disclose this
 16 information to the agency?
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: That's not my
 20 responsibility. I didn't know.
 21 BY MR. KELLER:
 22 Q. In this document they're talking
 23 about whether or not 3.7 will be medically
 24 okay and maybe defensible with the Office of
 25 Compliance. Do you know who would make the

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 2 decision whether or not 3.7 would be medically
 3 okay during this time frame?
 4 A. Well, Jerry Sadoff was
 5 probably -- and Dorothy Margolskee were
 6 probably making the assessment as they said
 7 here.
 8 Q. Here back on 549512, in the
 9 case -- "In case you want the details,
 10 Attachment #4 is a line listing of the lots -
 11 note column 5, which is the release dose per
 12 lot" --
 13 A. Where are we here?
 14 Q. On page 3 of the document which
 15 is 549512.
 16 A. Page 3, okay. And where?
 17 Q. Just where I left off reading.
 18 I'm just reading the next --
 19 A. Again.
 20 Q. In case you want the details,
 21 Attachment 4 is a line listing of the lots -
 22 note column 5, which is the release dose per
 23 lot and assume a 1 -- around a 1.1 log fall
 24 over 24 months. Do you see that?
 25 A. Yeah, I see that.

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 2 Q. If you go to 549518 of this
 3 document, it actually doesn't have a Bates
 4 number on it, but when we printed it out, the
 5 Excel printed with a number. This was also
 6 part of that document. It's a document
 7 entitled: "Total Doses on Low Mumps Titer
 8 Lots within Expiry." Do you see that?
 9 A. Uh-huh.
 10 Q. Here it says that US Doses
 11 Distributed in 2002 has 12,765,787. Do you
 12 see that?
 13 A. Yes, I see that.
 14 MR. SANGIAMO: In 2000.
 15 BY MR. KELLER:
 16 Q. In 2000, right.
 17 Is it fair to say that based on
 18 this attachment that what they're identifying
 19 here is the number of doses released in the US
 20 that had low potency below the 4.0 spec?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: No, I can't really
 24 see that here. It says, "Total Doses
 25 on Low Mumps Titer Lot within Expiry."

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2 So they would have been within expiry.

3 I'm not sure -- this is not -- there's

4 not sufficient labeling here for me to

5 tell what these are.

6 BY MR. KELLER:

7 Q. Fair enough. If you look at the

8 rest of the spreadsheet that's attached it

9 identifies for each lot, lot number, release

10 potency, expiry potency, package number, and

11 at the back of it it will identify the number

12 of lots that have been released for each --

13 number of doses in each lot. Do you see that?

14 A. Well, I'm not familiar with

15 these kinds of tables, so I -- I can see

16 what's labeled here. This is not --

17 Q. Do you recall --

18 A. There's a line total doses here

19 but there's nothing in it.

20 Q. That's after the first page. I

21 can represent to you without going back and

22 adding them up --

23 A. This is not -- this is

24 obviously spread out over several pages and

25 does not -- these are not labeled. So it's

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2 package doses, but I'd have to go back and

3 forth and relate them to something, if

4 they're even related.

5 Q. Let me ask you a question. Do

6 you recall during this time frame any

7 discussion about there being 10 or 12 million

8 doses that fell below the specification in the

9 label for end expiry?

10 A. Well, that's a lot of

11 assumptions. So what we're talking about so

12 far was a model, a stability model. It was

13 not saying that the doses fell below anything.

14 Q. Well, it's projecting that if

15 doses would fall below --

16 A. That's very different. That's

17 very different. That's a model is a model is

18 a model.

19 Q. Okay. Here Dorothy Margolskee,

20 she's a fairly senior executive at Merck.

21 Correct?

22 A. Very senior.

23 Q. Very senior. So she's

24 representing that this will be a compliance

25 issue with the agency. Correct?

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2 A. That obviously was her opinion.

3 Q. But you don't recall any

4 discussion about a compliance issue of tens of

5 millions of doses below end expiry projections

6 that were made by this model?

7 A. Not as you word it. I do

8 recall a discussion about mumps potency and I

9 do recall that there were discussions with

10 the agency as well, but I certainly don't

11 recall that anybody said -- certainly the

12 agency would be the one to tell us that there

13 were X number, million number of doses that

14 were out of compliance or released at the

15 wrong titer.

16 Q. When you say that there was

17 discussions about mumps potency with the

18 agency, were you involved in those discussions?

19 A. Probably not, certainly not as

20 far as they concerned -- involved manufacturing

21 issues.

22 Q. Were you involved in any

23 discussions where there was a discussion as to

24 what to tell CBER about these 106 doses at 4.0

25 and lower?

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2 MR. SANGIAMO: Object to the

3 form.

4 THE WITNESS: What do you mean

5 with what to tell CBER? We would have

6 shared data with them.

7 BY MR. KELLER:

8 Q. Did Merck tell CBER about these

9 106 lots?

10 A. How am I to know? As I said

11 before, that was not my responsibility.

12 Q. I understand that. Do you

13 recall any discussions regarding whether or

14 not to tell CBER about these 106 lots?

15 A. No, I do not. That was also

16 not my responsibility.

17 Q. Okay. Fair enough. Do you

18 recall any discussion about 227 lots that were

19 below 4.3?

20 A. No.

21 Q. Do you recall any discussion

22 about 227 lots with respect to anything?

23 A. The number doesn't strike a

24 bell at all.

25 MR. KELLER: Let me mark this

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 next exhibit as Exhibit 5.
 3 MR. SANGIAMO: 5?
 4 MR. KELLER: 6. I'm sorry.
 5 Strike that.
 6 Let me mark this next exhibit as
 7 Exhibit 6.
 8 - - -
 9 (Exhibit Schodel-6, E-mail
 10 chain, Bates MRK-KRA00549497 &
 11 00549498, was marked for identification.)
 12 - - -
 13 BY MR. KELLER:
 14 Q. For the record, Exhibit 6 is a
 15 document that bears Bates stamp number
 16 KRA 549497 through 498. It's a series of
 17 e-mails. I'll direct your attention to the
 18 e-mail that starts at the bottom of 5497 --
 19 549497 and runs on to the second page at 498.
 20 This one is from Timothy Schofield to Dorothy
 21 Margolskee, and it's talking about the "Low
 22 Months Target Lots within Expiry."
 23 A. Note that I was not copied on
 24 this e-mail.
 25 Q. Right, I see that. The e-mail

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 2 above that is from you. Do you see that?
 3 A. That's right.
 4 Q. Here it appears that you were
 5 responding to the e-mail that was below. So
 6 it looks like if you look at the February 22,
 7 2001, e-mail from Mr. Schofield to Margolskee,
 8 it was subsequently forwarded to you about
 9 40 minutes later. Do you see that?
 10 A. Okay. Now I get it. I just
 11 didn't understand.
 12 Q. Fair enough. I'm glad you
 13 pointed that out to me.
 14 If you look at Mr. -- who was
 15 Mr. Schofield again, what was his position?
 16 A. He was the head of biometrics
 17 at the time.
 18 Q. He was a statistician?
 19 A. Yes.
 20 Q. And Jonathan also?
 21 A. Not a clinical statistician. A
 22 biometrics person. So he was dealing with
 23 not clinical issues but manufacturing issues,
 24 analytical issues.
 25 Q. I see. Mr. Antonello, Joseph

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 2 Antonello, who is that?
 3 A. He was working in his group.
 4 He was also biometrician. Also not somebody
 5 who dealt with clinical statistics, but
 6 somebody who would work with the lab to
 7 validate assays and so on.
 8 Q. Did Mr. Hartzel and Mr. Antonello
 9 work together?
 10 A. I think actually Jonathan
 11 Hartzel was in the clinical statistics group,
 12 to which exact -- I mean, I was not in either
 13 of these two groups, so they may have worked
 14 together or not, I don't know.
 15 MR. SANGIAMO: Jeff, these guys
 16 are both doctors.
 17 MR. KELLER: Sure.
 18 BY MR. KELLER:
 19 Q. Dr. Hartzel, he's the one that
 20 was -- who worked on the planning subset data,
 21 correct, the unblinded subset data for
 22 Protocol 007?
 23 A. I don't know that for sure. He
 24 may have been the statistician associated to
 25 the study all of the sudden but whether he

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 2 has actually worked on that set of data other
 3 than summarize it, I don't know. There may
 4 have been other people in the background who
 5 worked on it. I did -- you're asking me
 6 things that I wouldn't know.
 7 Q. Sure. In here, in this e-mail
 8 from Schofield to Margolskee, Schofield says,
 9 "Dorothy, Here's the spreadsheet I was working
 10 from. A couple ideas:
 11 "1. I spoke with Joe Antonello
 12 who is doing the evaluation of the validation
 13 data..." Do you see that?
 14 A. Yeah.
 15 Q. Do you understand that this is
 16 the validation data for Protocol 007?
 17 A. No, I didn't.
 18 Q. You don't know?
 19 A. You're telling me now.
 20 Q. He suggested that we look at the
 21 dilution response profiles to see if the
 22 negatives were "marginal," or strictly flat.
 23 In addition, it could be interesting to see
 24 what the rates would be at 40 percent
 25 neutralization.

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 2 Do you see that?
 3 A. Yes.
 4 Q. He's talking about a
 5 neutralization assay. Correct?
 6 A. It would seem from here,
 7 because he mentions 40 percent neutralization,
 8 but out of context I wouldn't know.
 9 Q. Fair enough. Number 2 he says,
 10 "Would there be a better probability of
 11 success in retesting the failures (and some
 12 marginal positives) in the wild type neut."
 13 Do you see that?
 14 A. Yes.
 15 Q. The wild-type neut, that's
 16 Protocol 007's PRN assay. Correct?
 17 A. Uh-huh. I mean, this is a bit
 18 of jargon, so I -- in seeing the name, that's
 19 what I would expect, but I'm not sure. I
 20 don't know what he refers to exactly because
 21 he can do a wild-type neut with any wild-type
 22 mump strain.
 23 Q. So when they're talking about
 24 better probability of success in retesting
 25 that failures, how would you get a better

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 probability of success by retesting failures
 3 in a wild-type plaque reduction neutralization
 4 assay?
 5 MR. SANGIAMO: Objection.
 6 THE WITNESS: Well, failures in
 7 this context here, you know, means
 8 failures of performing in the assay so
 9 they are not -- so you don't have a
 10 valid data point for this particular
 11 sera which is, of course frustrating.
 12 They humanize people. They are sera.
 13 They've been analyzed, but for
 14 whatever reason the control was wrong,
 15 the cells were old, something else
 16 didn't work, so they're failures, test
 17 failures. Now the question is what
 18 are the values in these sera and you
 19 can --
 20 BY MR. KELLER:
 21 Q. You say the controls, do you
 22 recall there being any discussion about
 23 testing the failures in the preliminary subset
 24 of Protocol 007, the ones that didn't
 25 seroconvert?

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 2 A. I'm not sure what he means with
 3 failures here, whether those are failures
 4 that are failures because they are -- don't
 5 yield useful values or they're failures
 6 because they were wrongly classified, I'm not
 7 so sure.
 8 Q. Sure. If you look at the e-mail
 9 from you the same day, only an hour and a half
 10 later, again, cc'ing Hartzel, and in here you
 11 write, "Dear Tim, I think esp. 2 would be
 12 useful...." Esp. means especially 2?
 13 A. Yes.
 14 Q. What did you mean by "esp"?
 15 A. Yes.
 16 Q. So here you're saying retesting
 17 of the failures would be useful. Correct?
 18 A. Well, no. What I'm saying --
 19 yes and no. So what I'm saying really is it
 20 would be useful to have more data, more valid
 21 data. I'm making an argument that if you
 22 have a postimmunization -- a preimmunization
 23 titer that seems higher than the
 24 preimmunization titer -- the other way
 25 around. The preimmunization titer that seems

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 2 higher than the postimmunization titer,
 3 there's something funny going on. If you
 4 don't have data, you're actually -- you
 5 should retest and figure out whether there
 6 was something wrong.
 7 Q. I see.
 8 A. But, of course, you wouldn't do
 9 a retest just on those. Just the advantage
 10 of doing a retest is that it would also
 11 include those where you -- where something
 12 biologically not plausible is happening.
 13 Q. So would you not test vaccine
 14 failures in a PRN assay? Why don't you just --
 15 A. I'm still not sure whether
 16 we're talking about vaccine failures or not.
 17 Nobody says vaccine failures.
 18 Q. Let's go to the next e-mail from
 19 Jonathan Hartzel to you, Dr. Schodel, which
 20 happened about two minutes later. It says,
 21 this is from Hartzel, "I have given
 22 Emilio...," and that's Emilio Emini. Correct?
 23 A. Uh-huh.
 24 Q. He's running the lab that's
 25 running Protocol 007. Correct?

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2 MR. SANGIAMO: Object to the

3 form.

4 THE WITNESS: He was in charge

5 of the lab.

6 BY MR. KELLER:

7 Q. About 60 case numbers to retest

8 (the 42 failures and 17 marginal positives).

9 Do you see that?

10 A. Yes, I see that.

11 Q. I believe he will try to retest

12 them in both the ELISA (the wild-type mumps)

13 and the wild-type neut.

14 Do you see that?

15 A. Yes, I see that.

16 Q. Those are the two arms of

17 Protocol 007. Correct?

18 MR. SANGIAMO: Object to the

19 form.

20 THE WITNESS: I don't really

21 know what these failures refer to

22 here, whether they're failures in the

23 overall protocol that could be

24 including the control arm or whether

25 they would be any of the cells. This

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2 is just an assay issue. You have

3 serum samples in there which are low

4 and sometimes look like they can't

5 easily be interpreted, like the ones

6 below which have been higher before

7 they get immunized and then they're

8 lower, which is sort of strange. So

9 you wonder what's going on.

10 BY MR. KELLER:

11 Q. So during the middle of this

12 protocol, you're having the lab go back and

13 retest results from the protocol, whether

14 they're control failures or vaccine failures,

15 but you're retesting data that's --

16 A. I'm not having anybody do

17 anything. I did not direct anything or I

18 just expressed an opinion as to what kind of

19 data I would like to see. So in other words,

20 where it would be useful to get data now I --

21 you know, you can't just willy-nilly retest

22 stuff. So there has to be some protocol

23 followed, and that's the lab's problem, not

24 mine. I'm just reacting to whether this data

25 makes any sense.

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2 Q. So let me just direct your

3 attention to -- back to Exhibit 5, which is

4 the Margolskee e-mail. And an attachment at

5 549517, which is the preliminary subset

6 summary that Jonathan Hartzel is identified

7 on. Do you see that?

8 A. Yes.

9 Q. Now, if you look at the

10 seroconversion failures from the 4.9, the 4.0,

11 the 3.7, you'll see that there's ten failures

12 of the 4.9, there's 12 failures --

13 A. Wait a second. Where do I see

14 those?

15 Q. Looking at the percentages of

16 seroconversion, 159 over 169, 167 over 179,

17 149 over 169. That's how they're calculating

18 seroconversion, the total number by what

19 percentage of those seroconverted. Correct?

20 MR. SANGIAMO: Object to the

21 form. Dr. Schodel, do you see the

22 data to which Mr. Keller is referring?

23 THE WITNESS: I see the data,

24 but there's -- you're making an

25 assumption that I don't know which

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 ones are test failure. What I do see

3 here is the response rates that are

4 indicated here.

5 BY MR. KELLER:

6 Q. Right. So there's 169 kids in

7 the 4.9, 159 of those seroconverted. Right?

8 A. 159 of 169, that's right, yeah.

9 Q. If you actually run the number,

10 that's 94.1 percent. Does that make sense?

11 A. Yeah, that makes sense.

12 Q. So if you look at the failures,

13 159 out of 169, 10 kids didn't seroconvert for

14 4.9, 12 didn't seroconvert for 4.0 and 20

15 didn't seroconvert for 3.7. Do you see that?

16 A. Yes.

17 Q. That adds up to 42, doesn't it,

18 sir?

19 A. Yeah, it would.

20 Q. So does that help you to

21 understand the 42 failures that are listed

22 here that were given to the research lab

23 that's doing Protocol 007 to retest the 42

24 failures?

25 A. It also includes 17 margin

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2 positives. I hadn't made that connection,

3 but it may explain it.

4 Q. Why would you test in the middle

5 of an assay -- let me back up a second.

6 If the assay had not been

7 completely validated at this point, based on

8 your supervising clinical studies throughout

9 your 30-year career, what justification could

10 be done for going back and testing the

11 failures --

12 MR. SANGIAMO: Object to the

13 form. Calls for speculation.

14 MR. KELLER: I'm not done, Dino.

15 BY MR. KELLER:

16 Q. -- for testing the failures in

17 the middle of a clinical study before you

18 validated the study?

19 MR. SANGIAMO: Object to the

20 form. Calls for speculation.

21 THE WITNESS: There's a lot of

22 inherent assumptions in there. First

23 of all, what does validating the study

24 mean?

25 BY MR. KELLER:

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2 Q. Validating the protocol of

3 Protocol 007 for the PRN assay --

4 A. How would you do that?

5 Q. Don't they validate those assays

6 before they run them?

7 A. That's not the protocol.

8 That's the assay. The assay, I believe, was

9 validated.

10 Q. Was it validated before the

11 assay was started?

12 A. I would assume so, but I don't

13 know.

14 Q. Is that typically done?

15 MR. SANGIAMO: Object to the

16 form.

17 THE WITNESS: You're asking me

18 to speculate about what the lab did.

19 It was not my responsibility.

20 BY MR. KELLER:

21 Q. Sure. But is it fair to say

22 that in February 22nd, 2001, the lab was going

23 back and retesting the failures from the

24 seroconverting failures of Protocol 007?

25 MR. SANGIAMO: Objection. Calls

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2 for speculation.

3 THE WITNESS: I don't know that

4 from the e-mail. It was obviously

5 discussed. But whether they did it, I

6 don't know.

7 - - -

8 (Exhibit Schodel-7, 3/1/01

9 E-mail, Bates MRK-KRA00549218 &

10 00549219, was marked for identification.)

11 - - -

12 BY MR. KELLER:

13 Q. For the record, I've marked as

14 Exhibit 7 a document that has previously been

15 marked by Morsy --

16 MR. SANGIAMO: Exhibit 12.

17 BY MR. KELLER:

18 Q. -- Exhibit 12 which bears Bates

19 stamp number KRA 549218 through 219. Doctor,

20 I'd like you to take a minute to look at this

21 and see if you recall receiving this e-mail.

22 I'll represent that you're on one of the

23 listed.

24 A. I'm obviously copied on that.

25 I was -- you know, it's an invitation for a

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2 meeting. So I -- since I'm copied on it, I

3 probably received it and I probably -- I

4 don't remember this meeting at all. This was

5 a few years ago.

6 Q. That's fair. This was an e-mail

7 dated March 1, 2001, from Keith Chirgwin to a

8 whole host of people including yourself.

9 Correct?

10 A. Yes.

11 Q. The topic was "URGENT Mumps

12 expiry - Tomorrow's Teleconference." Do you

13 see that?

14 A. Yes.

15 Q. In the first -- there's a point

16 that says number "1-Preparation for RMC

17 discussion on March 8." Do you see that?

18 A. Yes, I see it.

19 Q. Do you know what RMC is?

20 A. I don't remember that acronym

21 anymore. It was some research management

22 committee or something, but I'm making this

23 up because I'm not sure what it means.

24 There's a lot of acronyms at Merck.

25 Q. Do you know what a recall

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 2 committee meeting is?
 3 A. Huh?
 4 Q. A recall committee meeting is?
 5 A. This is -- I don't think this
 6 is a recall meeting. But I don't know.
 7 Q. Fair enough.
 8 A. Recall meeting? I don't know.
 9 I don't think so.
 10 Q. I'm just asking if you --
 11 A. No.
 12 Q. Number 2 says, "Preparation for
 13 CBER stability discussion later this month."
 14 Do you see that?
 15 A. Yes.
 16 Q. Under "Agenda" it says, "MMD:
 17 Follow-up discussion with CBER - lots out of
 18 compliance." Do you see that?
 19 A. Yes.
 20 Q. It has Roberta McKee, Mike King
 21 and Mike Angelo. Do you see that?
 22 A. Yes.
 23 Q. Were those the people responsible
 24 for determining whether or not to disclose the
 25 lots out of compliance issue that we talked

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 2 about?
 3 A. As I said before, I don't know
 4 who was responsible, if there was a
 5 responsibility indeed. Roberta McKee was in
 6 regulatory on the CMC side, so on the
 7 manufacturing side, and Mike King was
 8 manufacturing, and Mike Angelo was in quality
 9 control and manufacturing as well.
 10 Q. These lots out of compliance,
 11 since this is contemporaneous with the memo
 12 that Ms. Margolskee -- is it Dr. Margolskee?
 13 MR. SANGIAMO: Dr. Margolskee.
 14 BY MR. KELLER:
 15 Q. Dr. Margolskee sent to the
 16 president of Merck as well as a bunch of other
 17 folks, do you understand that to be the same
 18 106 lots she was talking about?
 19 A. I don't know.
 20 Q. You don't know. If you look on
 21 the next page under "Clinical," number 1 it
 22 says, "Clinical support for end of shelf life
 23 titers." Do you see that?
 24 A. Yes.
 25 Q. Under 5 it says, "Jerry Sadoff."

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 And under 6 it says you, Dr. Schodel.
 3 Do you see that?
 4 A. Yes.
 5 Q. Number 2 it says, "plans for
 6 assessment and possible need for rescue."
 7 What did you mean by that? What do you
 8 understand that to mean?
 9 MR. SANGIAMO: Objection.
 10 THE WITNESS: I have no idea.
 11 MR. SANGIAMO: The question is
 12 what do you understand that to mean?
 13 MR. KELLER: Yes.
 14 THE WITNESS: Assessment -- I
 15 mean, rescue would mean revaccination,
 16 I guess, if there was any rescue
 17 needed, but I don't know what was
 18 meant here.
 19 BY MR. KELLER:
 20 Q. You don't know. Okay. Fair
 21 enough.
 22 MR. KELLER: Mark Exhibit 8.
 23 - - -
 24 (Exhibit Schodel-8, PowerPoint
 25 presentation, Bates MRK-CHA00086318,

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 was marked for identification.)
 3 - - -
 4 BY MR. KELLER:
 5 Q. For the record, Exhibit 8 is a
 6 document that bears Bates stamp number 86318,
 7 and it's a three-page presentation document.
 8 And I'll tell you from the metadata produced,
 9 this is dated March 3, 2001. And my note
 10 identifies this as being used at the 3/8
 11 teleconference.
 12 A. Is that the entire presentation?
 13 Q. Yes. Can you tell me if you
 14 recall ever seeing this presentation before?
 15 MR. SANGIAMO: Dr. Schodel, you
 16 don't have to accept Mr. Keller's
 17 representation that he just made to
 18 you about being the entire
 19 presentation and the date. I'm not
 20 saying he's wrong, but you don't have
 21 to accept it.
 22 MR. KELLER: Are you saying the
 23 metadata is false?
 24 MR. SANGIAMO: No, I'm not
 25 saying that it is false. I haven't

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 2 seen the metadata. Sitting here right
 3 now, I can't -- I don't know what the
 4 metadata says.
 5 THE WITNESS: I don't remember
 6 the details, but I can read it, of
 7 course.
 8 BY MR. KELLER:
 9 Q. Sure. Focus on the first page.
 10 A. Okay.
 11 Q. Stability data do not support
 12 current end of shelf life (4.3 log). Do you
 13 see that?
 14 A. I see that.
 15 Q. Does this help refresh your
 16 memory at the time of this presentation that
 17 the shelf life label claim was 4.3 log?
 18 A. That's what is stated here.
 19 Q. Do you recall there being a
 20 meeting that discussed that the stability data
 21 did not support the current end of shelf life
 22 label claim of 4.3?
 23 MR. SANGIAMO: Objection.
 24 THE WITNESS: I now remember
 25 that I was in a meeting with this

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 2 topic because you just showed me the
 3 agenda so, yes, I do, I can read.
 4 BY MR. KELLER:
 5 Q. Do you recall any discussion
 6 that happened at that meeting?
 7 A. Not in any detail.
 8 Q. Does this help refresh your
 9 memory of seeing this document in the past?
 10 A. No.
 11 Q. The second bullet point says,
 12 "Further increase in release potency is not
 13 feasible...", and it says, "... (target 5.2)."
 14 Do you see that?
 15 A. Yes, I see that.
 16 Q. Do you recall any discussion
 17 during this time frame of March of 2001 about
 18 looking at whether or not Merck could overfill
 19 even further than what it did in 1999?
 20 A. I don't recall such a discussion,
 21 but I would support the statement.
 22 Q. The last bullet point,
 23 "Therefore we must provide clinical data to
 24 support a decrease in the labeled potency."
 25 Do you see that?

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 2 A. I see that.
 3 Q. That data, that's Protocol 007
 4 with a release -- with a potency below 4.3,
 5 either 4.0 or 3.7. Correct?
 6 A. I'm not sure entirely because
 7 this is a different time here. This was --
 8 when did this happen? I mean --
 9 Q. The date on the document says --
 10 the metadata which is the computerized
 11 data that comes --
 12 A. We're talking about 2001.
 13 Q. Yes.
 14 A. Which was when that protocol
 15 was being run. Right?
 16 Q. Correct.
 17 A. So it's not -- it wasn't
 18 planned for that purpose.
 19 Q. But was it used for that purpose?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 BY MR. KELLER:
 23 Q. Let me back up. What was the
 24 purpose of -- you say it wasn't planned for
 25 the purpose. What was the purpose Protocol

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 2 007?
 3 A. I said that before. It was to
 4 provide clinical data to support what now had
 5 changed in the labeling expectations, a
 6 scientifically supported end expiry number.
 7 Q. And so in what they were -- what
 8 was in Protocol 007 was a release dose of 4.9
 9 and two lower doses. And two of those lower
 10 doses were below 4.3. Correct?
 11 A. That's correct.
 12 Q. So they were trying to change
 13 the label to reduce the potency claim in the
 14 label from 4.3 to either 4.0 or 3.7. Correct?
 15 A. Yeah, but you're bringing these
 16 two things that are both timely and logically
 17 not necessarily related into relation. The
 18 protocol was run for what I said it was run
 19 for. Now the data were available. So when
 20 there was a -- at least an impression of an
 21 issue with a stability model, of course, the
 22 data as any other data out in the market,
 23 were used to understand the behavior of the
 24 vaccine across its potency range. That's a
 25 post hoc use of the data. It is not why this

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 2 was run, because quite obviously -- I mean,
 3 this happened in 2001, the protocol was
 4 already under way, so it was not planned or
 5 designed for this particular purpose.
 6 Q. But it certainly increased the
 7 importance of that protocol having a reduced
 8 potency from 4.3 to either 4.0 or 3.7. Correct?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: At least
 12 temporarily, yes, because now there
 13 were data that could be supplied
 14 which -- and often not available in
 15 these kinds of situations.
 16 - - -
 17 (Exhibit Schodel-9, 9/28/01 E-mail
 18 with attachment, Bates MRK-KRA00561416
 19 - 00561421, was marked for identification.)
 20 - - -
 21 BY MR. KELLER:
 22 Q. Let me mark as Exhibit 9 a
 23 document bearing Bates stamp number 561416
 24 through 21. And here there is a -- it's an
 25 e-mail with an attachment. The e-mail is from

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Jonathan Hartzel to a laundry list of folks
 3 including you, Dr. Schodel.
 4 Can you tell me, if you take a
 5 minute to take a look at this and tell me if
 6 you recognize the e-mail and the attachment as
 7 well?
 8 A. There's a lot of information in
 9 here, so while I can quickly read it, it
 10 doesn't mean that I'll be able to answer to
 11 all details.
 12 Q. Do you recall seeing this e-mail
 13 and attachment?
 14 A. Not this specific one, but I do
 15 remember that a discussion about the ELISA
 16 cutoff at some point happened.
 17 Q. That discussion about the ELISA
 18 cutoff, we're talking about the cutoff of the
 19 wild-type ELISA assay used in Protocol 007?
 20 A. Uh-huh.
 21 Q. What is a cutoff?
 22 A. A cutoff is a number that with
 23 reasonable certainty distinguishes between
 24 positives and negatives.
 25 Q. When you say "between positive

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 2 and negative," is that for purposes of the
 3 ELISA assay used in Protocol 007, used to
 4 determine whether or not the results are
 5 treated as a seroconversion?
 6 A. Yeah, it would be for the
 7 purpose of a seroconversion and to determine
 8 whether somebody has preexisting antibodies
 9 or postvaccination antibodies. The two are
 10 linked, of course.
 11 Q. You talked earlier, there's two
 12 ways to analyze ELISA assays. One was by
 13 using a fixed cutoff and the other one was
 14 using a fold criteria?
 15 A. Right.
 16 Q. Fourfold criteria?
 17 A. Right.
 18 Q. So is it fair -- let me just
 19 kind of go through this e-mail. Here the
 20 subject is CBER background ELISA. During the
 21 CAS -- strike that.
 22 "During CAS and at some
 23 follow-up meeting, some additional clinical
 24 information was request to address some areas
 25 of concern."

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 2 The CAS, that's the clinical
 3 assay subteam committee. Correct?
 4 A. I think so, yeah.
 5 Q. Were you a member of that?
 6 A. Yes.
 7 Q. Were you the head of that
 8 committee?
 9 A. At some point, yes.
 10 Q. During this period --
 11 A. Or co-chair anyway.
 12 Q. During the September of 2001
 13 were you the co-chair or head of this
 14 committee?
 15 A. Probably. Not so good with the
 16 time exactly.
 17 Q. What was the purpose of this
 18 committee?
 19 A. Was to review the status. The
 20 major purpose was an operational one. It was
 21 to make sure that we actually could do the
 22 assays that we needed to be done in time. So
 23 we had a lot of assay throughput because of
 24 Gardasil, because of ProQuad and so on. So
 25 we had tens of thousands of assays that were

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 2 not being done in time. We had to come up
 3 with a better way to manage that. That was
 4 the major purpose why we started this
 5 committee and then we on occasion also looked
 6 at specific questions around the assays as
 7 they concerned any one of the participants,
 8 whether that was clinical or regulatory or
 9 the lab.
 10 Q. So do you recall a discussion at
 11 the clinical assay subcommittee regarding the
 12 setting of what standard would be used to
 13 determine a seroconversion with the ELISA
 14 assay used in Protocol 007?
 15 A. No. I do vaguely remember that
 16 the discussion that is represented here
 17 happened that it was set, and that I don't
 18 think we had pre-discussed how to set it in
 19 that particular committee. At least I don't
 20 remember it. And that CBER wanted more
 21 information about its behavior in classifying
 22 sera and that information was provided. Then
 23 the information that was available was
 24 discussed obviously as it is attached here.
 25 Q. So here in these the second --

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 2 these areas where it says, "...to address some
 3 areas of concern," it says, "This information
 4 was not to be sent to CBER, but was for our
 5 own understanding." Do you see that?
 6 A. Yeah.
 7 Q. So was that typical at Merck, to
 8 discuss information that would be a concern
 9 and not provide that information to CBER?
 10 A. There was nothing to provide to
 11 CBER because the area of concern is the
 12 debate that was ongoing at CBER at the time
 13 as well as to whether an absolute cutoff was
 14 okay or whether you should apply fourfold
 15 criteria and all kinds of permutations in
 16 between which can cause more confusions than
 17 anything else. The same discussion about
 18 Varicella and about other assay. I don't
 19 recall any specific issue with mumps. And,
 20 of course, in addressing these kinds of -- in
 21 CBER there were two schools of thought.
 22 There were those who wanted to have fourfold
 23 criteria and those who were okay with the
 24 cutoff and had been taking part in these
 25 cutoff discussions and how they were to be

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 2 used.
 3 So we had similar discussions
 4 about a number of assays. So the concern was
 5 whether we could come to a common
 6 understanding. In order to do that, we had
 7 to look at the data. That's not something
 8 that was not shared with CBER because it
 9 wouldn't have been shared with CBER. In
 10 fact, the e-mail below tells you that it has
 11 actually been faxed to CBER. So data
 12 was faxed to CBER --
 13 Q. That's a different -- that
 14 attached something different.
 15 MR. SANGIAMO: Mr. Keller, you
 16 got to let him finish his answers.
 17 MR. KELLER: Sure.
 18 MR. SANGIAMO: So what's the
 19 pending question?
 20 THE WITNESS: But the value of
 21 the -- I mean the data themselves
 22 would have been discussed internally
 23 before they were sent off. Besides
 24 these are -- these are -- this is all
 25 based on just assay data that have not

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 2 been cleaned or screened so they would
 3 never been used for clinical
 4 submission. They would not be -- they
 5 would not send to an agency data you
 6 do not consider final data because
 7 they have not been cleaned or
 8 screened. That would be actually not
 9 in compliance. So why should they be
 10 shared with CBER. There's no reason
 11 to.
 12 Now I have to share something
 13 with you. I need a break.
 14 MR. KELLER: Sure.
 15 VIDEOGRAPHER: Off the record at
 16 2:11. This will end disc number
 17 three.
 18 - - -
 19 (A recess was taken.)
 20 - - -
 21 VIDEOGRAPHER: Back on the
 22 record at 2:19. Beginning of disc
 23 number four.
 24 BY MR. KELLER:
 25 Q. Dr. Schodel, if you look on the

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 2 e-mail that you received attaching this Mu
 3 Dist plus Mu Me Pre-Pos Rates.doc, it says,
 4 Attached is a memo which contains information
 5 on the distribution of 6 week mumps titers
 6 based on mumps wild-type ELISA assay (with
 7 special interest in those falling between 10
 8 and 40).
 9 Do you recall discussions
 10 regarding whether or not setting the
 11 serostatus cutoff for the ELISA arm of
 12 Protocol 007 as to whether or not the
 13 serostatus cutoff should be set between those
 14 ranges of 10 and 40?
 15 MR. SANGIAMO: Object to the
 16 form.
 17 THE WITNESS: I do not recollect
 18 such discussions.
 19 BY MR. KELLER:
 20 Q. Do you know -- so you don't know
 21 the special interest in those fall in between
 22 those 10 and 40 range?
 23 A. No, you asked me a different
 24 question. So ask the question again.
 25 Q. Sure. Do you recall -- so you

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 2 don't recall what the special interest
 3 identified in this particular e-mail the
 4 writer had with respect to the cutoff arm
 5 between 10 and 40?
 6 MR. SANGIAMO: Object to the
 7 form.
 8 THE WITNESS: I can deduce it
 9 from the rest of the e-mail. So could
 10 you. It goes back to this discussion
 11 of whether a fourfold rise is
 12 important or it should be applied on
 13 top of a serostatus cutoff. Because
 14 these things were not completely
 15 worked out by the time of this
 16 meeting, we had to take into account
 17 what would happen if a fold rise would
 18 apply even though the serostatus
 19 cutoff in our eyes was the right thing
 20 to do.
 21 BY MR. KELLER:
 22 Q. I see. Was there a concern, do
 23 you recall -- you said that you're deducing
 24 from that. Do you recall any specific
 25 conversations at Merck during this time frame

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 2 regarding the setting of the serostatus cutoff
 3 at a range between 10 and 40?
 4 A. No.
 5 Q. Do you recall there being any
 6 discussion about the serostatus cutoff of 10
 7 being too low?
 8 A. No.
 9 Q. Do you recall there being any
 10 concern that CBER would want to see a higher
 11 serostatus cutoff?
 12 A. No, not in this particular way.
 13 You have to go back to what we discussed
 14 before which is the mixing of these two
 15 criteria.
 16 Q. Gotcha. So at this point in
 17 time there hadn't been a determination as to
 18 what criteria would be used, whether the
 19 serostatus cutoff, a fixed cutoff or one
 20 with -- that's based on a fourfold criteria.
 21 Correct?
 22 A. No. It had been determined
 23 that a serostatus cutoff would be used. So a
 24 fixed cutoff. That is what was submitted to
 25 CBER and what was -- how the assay was run.

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 2 CBER on the other hand, was apparently still
 3 struggling with the concept and some people
 4 wanted, in addition, to apply a fold rise
 5 criteria. That message was the serostatus
 6 cutoff because now you have to figure out
 7 what would that mean in terms of
 8 classification because you're not changing
 9 your serostatus cutoff but you're adding a
 10 different criterion and it changes how you
 11 classify things.
 12 Q. So if you hit a serostatus
 13 cutoff of -- if you set it at, for example,
 14 ten, there was a concern that you'd also have
 15 a fourfold increase between the pre and the
 16 post?
 17 A. That's right. And if you were
 18 to do that, then obviously you would lose
 19 quite a bit of the population that fall in
 20 between these two because you could no longer
 21 determine whether they were seroconverting.
 22 So that would change the population in your
 23 trial.
 24 Q. And the people that were leaning
 25 towards doing a fourfold analysis were the

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 2 folks at CBER. Correct?
 3 A. It came back several times from
 4 CBER. I think it's more -- I don't know
 5 exactly who it was, but I think it's more the
 6 old school thought of because that's what
 7 we've done all the time. And then eventually
 8 it changed.
 9 Q. Let's turn your attention to the
 10 attachment to this e-mail which is 561418.
 11 A. Yes.
 12 Q. Here it says, "Distribution of
 13 6-week Mumps Titers Using the Mumps Wild-type
 14 ELISA Assay." Do you see that?
 15 A. Yes.
 16 Q. This wasn't attached to CBER.
 17 Correct?
 18 A. I don't know --
 19 MR. SANGIAMO: Object to the
 20 form.
 21 THE WITNESS: -- whether it was
 22 attached to CBER, so I couldn't tell
 23 you.
 24 BY MR. KELLER:
 25 Q. It's not in the listing of the

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 2 e-mail that's below --
 3 A. As it states in this e-mail
 4 here, these are uncleaned and screened data
 5 so they would not be submitted as such to
 6 CBER.
 7 Q. Here it says, "M-M-R® II
 8 Protocol 007 and ProQuad® Protocol 012 are
 9 currently the only studies in which the new
 10 mumps wild-type ELISA assay has been performed."
 11 Do you see that?
 12 A. Uh-huh.
 13 Q. These were a new assay.
 14 Correct?
 15 A. Yes.
 16 Q. "For this assay the seroprotective
 17 level is defined to be 10 Ab units."
 18 Do you see that?
 19 A. Yes.
 20 Q. When it says "seroprotective,"
 21 what do you understand that to mean?
 22 A. Well, that's actually a little
 23 bit of mislabeling. It's the seropositive
 24 level.
 25 Q. I see. So it's not identifying

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 2 whether or not it can protect a kid from
 3 getting -- the kid has more --
 4 A. There is no absolute cutoff
 5 that the would protect anybody. Even a
 6 higher titer wouldn't necessarily protect
 7 them.
 8 Q. So the cutoff is not tied to
 9 whether or not -- for this ELISA assay,
 10 whether or not it will protect kids from
 11 getting mumps. Right?
 12 A. No. No.
 13 Q. Subjects who have titers of than
 14 less than 10 Ab units are considered negative.
 15 Do you see that?
 16 A. Yes.
 17 Q. So those folks, if you have a 10
 18 Ab cutoff -- if you had -- if the results of
 19 this assay were below 10 Ab, that would be a
 20 seroconversion failure. Right?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: No. If you have a
 24 titer initially of 8 and you have 200
 25 afterwards, that's a seroconversion.

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 2 If you have a titer initially of 12
 3 and you now have a titer of 8, that's
 4 not a seroconversion.
 5 BY MR. KELLER:
 6 Q. That's a pre-positive?
 7 A. That's where a problem
 8 potentially could be. Or if you have a titer
 9 of 8 and 8, that's also not a seroconversion.
 10 But anything goes from below 10 or above 10
 11 is a seroconversion.
 12 Q. Gotcha. And that's what --
 13 you're converting -- the blood is converting
 14 from one state to another. Correct?
 15 A. That's right. That's why it's
 16 a classification, it's a little different
 17 from the fourfold criteria.
 18 Q. So here in this document it
 19 says, There is some concern that CBER may
 20 require a fold rise in titers (from
 21 pre-negative to postvaccination) in order to
 22 demonstrate that seroconversion has occurred.
 23 So that a subject who has a prevaccination
 24 titer of 9.9 and a postvaccination titer of
 25 10.1 (the difference being within the

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 2 variability of the assay) would not be
 3 considered a seroconverter.
 4 Do you see that?
 5 A. That's correct.
 6 Q. But for the end result was that
 7 a fourfold analysis wasn't done. Correct?
 8 A. No.
 9 Q. So under Merck's analysis, if
 10 their prevaccination titer and their wild-type
 11 ELISA assay was 9.9 and postvaccination titer
 12 was 10.1, that would be a seroconverter?
 13 A. Yes.
 14 Q. When it says that is the
 15 difference being -- "the difference being
 16 within the variability of the assay," is
 17 that -- does that mean that those results
 18 could switch each time you ran the assay?
 19 A. That's right. But, of course,
 20 they do that in both ways, because it's the
 21 variability of the assay. So you will also
 22 have people who are pre-positives. In other
 23 words, they're not considered, and then they
 24 become seronegative.
 25 Q. If the analysis show that they

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 2 were all going in one direction, would that
 3 cause you concern?
 4 MR. SANGIAMO: Objection to the
 5 form.
 6 BY MR. KELLER:
 7 Q. Like the variability, if, you
 8 know, instead of being -- balancing out -- the
 9 disgruntle results balancing out --
 10 A. It's a theoretical question.
 11 In any assay if everything goes in one
 12 direction, you would try to analyze why that
 13 is. It doesn't necessarily mean it's wrong.
 14 There could be reasons for it. But it's
 15 something that you want to look at. But it
 16 doesn't apply here.
 17 MR. SANGIAMO: Objection to the
 18 form of that last question. Thank
 19 you.
 20 BY MR. KELLER:
 21 Q. Do you recall doing any analysis
 22 as to the results of Protocol 007 to see
 23 whether or not the fourfold criteria would
 24 have changed the results?
 25 A. I don't remember that. But in

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 2 general I think when such requests came in,
 3 we would do an analysis of what it would do
 4 to the results. But there is an additional
 5 difficulty with that. It's not just that it
 6 changes the results. It also changes the
 7 population that you identify because now
 8 everybody who is between 10 and 40 falls out.
 9 So there's a number of things, number of
 10 consequences to consider. So all the people
 11 who actually have responded but at a lower
 12 rate are no longer considered. Not that
 13 that's -- it's not a big population here,
 14 but...
 15 Q. But isn't the purpose of setting
 16 the -- here it says seroprotective level, but
 17 the serostatus cutoff is to identify some
 18 immunological response in the blood to the
 19 antibodies that would lead to a conclusion
 20 that the kid will be protected from getting
 21 the mumps virus?
 22 MR. SANGIAMO: Object to the
 23 form.
 24 THE WITNESS: Those are two
 25 different concepts. First of all, the

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 2 primary and most important part is
 3 that you said a cutoff in a way that
 4 it relatively reliably and repeatedly
 5 allows you to distinguish between two
 6 different populations, those that have
 7 seroconverted and those that have not
 8 seroconverted. The question as to
 9 whether that's related to protection
 10 or not is not one that entered here at
 11 all because there is no efficacy study
 12 attached to it.
 13 BY MR. KELLER:
 14 Q. Right. CBER didn't require any
 15 sort of analysis to sort of link the
 16 serostatus cutoff to something that relates to
 17 the vaccine at that level protecting the kid
 18 from getting sick?
 19 MR. SANGIAMO: Object to the
 20 form.
 21 THE WITNESS: There is no
 22 efficacy trial that that could have
 23 been related to. However, on the
 24 population basis, a vaccinated
 25 population has a very low likelihood

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 2 of acquiring mumps.
 3 BY MR. KELLER:
 4 Q. What's your basis for that?
 5 A. Epidemiology, look at the
 6 curves. There's almost no mumps in the
 7 United States.
 8 Q. How do you explain the outbreaks
 9 that occurred in 2006, 2009 and currently?
 10 A. It's not perfect protection but
 11 it's a protection that has reduced the level
 12 by several hundred folds.
 13 Q. You do have to admit the vaccine
 14 is not performing as well as it did in the
 15 past?
 16 A. No, I don't have to admit that
 17 at all.
 18 Q. You think it works perfectly the
 19 same as it did back when Dr. Hilleman ran
 20 those assays?
 21 A. Yes, I do.
 22 Q. Do you sit here today and think
 23 that the vaccine protects 96 percent of the
 24 kids who get the vaccine?
 25 A. That's -- I don't know that

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 2 exact number. But it certainly -- whatever
 3 the number was then, which has some
 4 uncertainty around it, too, because of how
 5 the trials were run, I would consider under
 6 the same circumstances that to be still the
 7 same.
 8 Q. I see. Have you seen any
 9 studies conducted by Merck that showed that
 10 the vaccine performed significantly lower than
 11 96 percent --
 12 A. That the vaccine performance --
 13 Q. -- by neutralizing studies? Let
 14 me strike that.
 15 Have you ever seen any assays
 16 conducted at Merck with respect to the mumps
 17 vaccine by a plaque reduction neutralization
 18 assay that showed the seroconversion to be
 19 below 80 percent?
 20 A. Not a formal study, no.
 21 Q. If it's not a formal study, then
 22 what kind of study did you see?
 23 A. I remember that both from
 24 conversations within Merck but also from
 25 conversations with people at the NIH and

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 2 other institutions, that different mumps
 3 strains react differently in the neuts assay.
 4 So if you use a different strain and if you
 5 use different conditions, you can see
 6 seroconversion rates that are different with
 7 the same set of sera. It has nothing to do
 8 with Merck. That's just a general fact of
 9 the neutralization assay.
 10 Q. Who do you recall speaking with
 11 at NIH?
 12 A. Rubin, Dr. Rubin.
 13 Q. And when was that?
 14 A. Oh, I don't know.
 15 Q. Last year?
 16 A. No, no.
 17 Q. 20 years ago?
 18 A. It was certainly more around
 19 the time of the -- of an outbreak probably or
 20 an investigation into an outbreak.
 21 Q. So in the 2006, 2009?
 22 A. Yeah, that may be the right
 23 time.
 24 Q. In regards to 2006 or 2009?
 25 A. No, I don't. I said 2009

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 2 certainly not.
 3 Q. Sometime around 2006?
 4 A. Yeah.
 5 Q. Were these studies ever
 6 conducted by Merck or studies conducted by
 7 CBER?
 8 A. What do you mean by "these
 9 studies"?
 10 Q. These discussions you talked
 11 about, were those studies --
 12 A. Well, at the time --
 13 MR. SANGIAMO: Just a minute,
 14 Dr. Schodel, let Jeff finish his
 15 question.
 16 BY MR. KELLER:
 17 Q. These studies, these conclusions
 18 that different viruses will have different
 19 seroconversion rates based on a plaque
 20 reduction neutralization assay, were these
 21 assays that you discussed, were these run by
 22 Merck or were they run by somebody else --
 23 MR. SANGIAMO: Object to the
 24 form.
 25 BY MR. KELLER:

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2 Q. -- when you talked to Mr. Rubin,

3 Dr. Rubin?

4 A. I think both at Merck and at

5 the NIH there were mumps neutralizing assays

6 performed with different strains. At the

7 time there was a question as to whether

8 outbreaks might be due to strains with

9 different characteristics, different genetic

10 sequences, different virulents. So various

11 labs tried to figure out what the basis of

12 these apparently high out attack rates in

13 certain populations were. And in the context

14 of that other strains were tried as well.

15 Q. Do you know which strains were

16 tried?

17 A. No, no idea.

18 Q. Let me direct your attention

19 back to Exhibit 9 in the attachment 561418.

20 Here it says in the second paragraph, "Due to

21 the characteristics of the mumps wild-type

22 assay, it will be very difficult to accurately

23 read titers below 10 Ab units."

24 Do you see that?

25 A. Yes.

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2 Q. If the serostatus cutoff is set

3 at 10, is there a concern that that assay

4 can't read below 10?

5 A. Well, there is a concern if you

6 apply a fourfold criterion. Because in order

7 to apply a fourfold criterion with a 10

8 cutoff, you need to be able to read down to

9 2.5 accurately. That may not be possible,

10 technically not be possible.

11 Q. Well, that's a question of

12 dilution, isn't it?

13 A. No, it's a question of the

14 sensitivity of the assay. You can dilute as

15 much as you want. As you dilute, you also

16 dilute the antibody. You may get rid of some

17 background, but you don't necessarily gain

18 sensitivity.

19 Q. I see. So wouldn't that be an

20 argument for increasing the cutoff?

21 A. As I said before, you can't see

22 these things in isolation. Yes, if you

23 wanted to use a fourfold criterion which I

24 think would be inappropriate for this kind of

25 an assay by today's standards, then it would

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2 be an argument. But then you would get into

3 the other problem that you misclassify people

4 who are actually seropositive into being

5 seronegative. So it's a decision that has to

6 do with the classifications. And you would

7 change whom you call positive and whom you

8 call negative.

9 Q. I'm just trying to understand

10 how you set a cutoff, serostatus cutoff. If

11 it's not linked to whether or not it protects

12 the kid, then what are you linking that cutoff

13 at? It seems arbitrary.

14 MR. SANGIAMO: Object to -- what

15 is your question?

16 BY MR. KELLER:

17 Q. Is that cutoff, is it arbitrary

18 if it's not set to some ability to protect a

19 kid, if you're going to use an assay that

20 reports in seroconversion, and that

21 seroconversion is based on a static cutoff,

22 and that cutoff is not set to anything as to

23 whether or not it's going to protect a kid

24 from getting sick, I'm just trying to

25 understand, how do you set the cutoff? What's

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2 the basis for setting it?

3 MR. SANGIAMO: Object to the

4 form.

5 THE WITNESS: I think I said

6 that several times. The basis is a

7 simple classification of positives and

8 negatives. You can set it at

9 different points and you will have

10 different classifications. And they

11 have -- they inherently have different

12 errors relative to the assay and

13 potentially relative to outcomes. But

14 this particular assay and the outcomes

15 are not linked in any meaningful

16 manner. So I can't say that on

17 protection rates because I don't know

18 what they are. And besides, it's been

19 observed in mumps that there isn't an

20 absolute cutoff for protection,

21 otherwise we probably would have

22 cutoffs. In other words, there is not

23 a titer that you're completely

24 reliably protected.

25 BY MR. KELLER:

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2 Q. So these errors that you're

3 talking about, are these at all related to --

4 let me strike that.

5 What do you mean by "errors"?

6 You just referred to the errors in the

7 classifications.

8 A. Well, errors in classification

9 would be if you had a crystal ball and you

10 could tell the absolute truth of who has an

11 antibody and who doesn't have an antibody

12 even below the detection limit of an assay,

13 which, of course, you can't, then you would

14 falsely classify some by one cutoff and

15 others by another cutoff. But you don't --

16 since you need a third, as they say in

17 philosophy, tertium non datur, there is no

18 third to compare it to. So you don't have an

19 absolute measure and therefore, the -- there

20 is always a degree of arbitrariness to

21 setting a serostatus cutoff, to use your own

22 words. However, it is based on some

23 scientific principles which is you can

24 reliably distinguish seronegatives and

25 seropositives and you can reliably

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2 distinguish those who will respond and those

3 who will not respond. And that's good enough

4 for this kind of an assay.

5 Q. I see. Here in this memo, they

6 state, "the difference being within the

7 variability of the assay." If the variability

8 of the assay falls below -- if you set it at

9 10, the variability can run below 10, then you

10 may have assays that have errors around that

11 variability?

12 MR. SANGIAMO: Objection to

13 form.

14 THE WITNESS: That would be true

15 for any cutoff in any form of

16 seroconversion rate you apply because

17 there's always an error around any

18 cutoff and any criterion and you will

19 always have something that falls

20 within the error. The art is to be

21 reasonably outside of the error with

22 the majority of your samples.

23 BY MR. KELLER:

24 Q. Later on in this document it

25 says in the last paragraph, it says, If CBER

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2 required a 4-fold rise in titers (defined as

3 less than 10 to greater than equal to 40), the

4 seroconversion rate for these studies would

5 range from 80.9 percent to 85.2 percent.

6 Do you see that?

7 A. Yes.

8 Q. That range is based on the

9 different potencies in the protocol for the

10 wild-type ELISA. Correct?

11 A. Well, I assume that. I don't

12 know that for sure. It could also be a

13 different analysis that he performed. I

14 mean, it's clear the more people you exclude

15 from the analysis, the more you change the

16 outcome.

17 Q. I see. So was that one of the

18 concerns that they're talking about here, is

19 that if CBER required this fourfold rise, that

20 the seroconversion rate would, in fact, be

21 lower than reported with the fixed 10 Ab

22 cutoff?

23 MR. SANGIAMO: Objection.

24 THE WITNESS: I can't speculate

25 as to that. That would have been a

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2 consequence of what we thought at the

3 time was not the right thing to do. I

4 think CBER concurred in the end.

5 MR. KELLER: Let's mark this

6 next exhibit as Exhibit 10.

7 - - -

8 (Exhibit Schodel-10, E-mail chain,

9 Bates MRK-KRA00561361 - 00561365-00017,

10 was marked for identification.)

11 - - -

12 BY MR. KELLER:

13 Q. For the record, Exhibit 10 is a

14 document that bears Bates stamp number 561361

15 through 561365 which includes a PowerPoint

16 presentation at 561365 through -- there's 17

17 pages of this presentation.

18 A. I have two different ones here.

19 Q. One is -- I'm sorry. Let's pull

20 the one of them. The 19058 you can just get

21 rid of. It's the same document. We

22 previously marked 19085 in Morsy as

23 Exhibit 20. I'm going to use this copy

24 because it's attached to an e-mail that went

25 to Dr. Schodel. So if that helps.

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 2 MR. SANGIAMO: Actually it
 3 doesn't. 19085 that's out of play
 4 right now.
 5 MR. KELLER: That's out of play.
 6 I'm just -- for the record, that
 7 document was used in Schodel [sic] and
 8 it's the same presentation but this
 9 one was attached to an e-mail that
 10 went to Dr. Schodel.
 11 BY MR. KELLER:
 12 Q. So for the record, on
 13 January 18, 2002, there is a doc -- subject of
 14 this e-mail is CRRC Agenda - 22 January, 2002.
 15 And, Dr. Schodel, you received this and was
 16 sent by Dr. Chirgwin. Do you see that?
 17 A. Yes.
 18 Q. Can you take a minute and look
 19 at this presentation and tell me if you recall
 20 seeing this presentation? I'm not going to
 21 ask you about every page, but you're welcome
 22 to look at it.
 23 A. Okay.
 24 Q. If you look on the e-mails that
 25 attach this particular PowerPoint, there's an

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 2 e-mail from Jeffrey C-H-O-D-A-K-E-W-I-T-Z to
 3 you as well as a bunch of other folks
 4 including Emilio Emini and it's talking about
 5 the CRRC agenda. Here it says, Have you seen
 6 draft overheads for the mumps assay issue?
 7 Has the variability of the current status or
 8 contingency of extended commitment to 4.3 been
 9 discussed -- addressed by MMD --
 10 A. Sorry, viability.
 11 Q. Sorry. Viability. "Has the
 12 viability of the current status or contingency
 13 of extended commitment to 4.3 been addressed
 14 by MMD?"
 15 And then you responded, "Dear
 16 Jeff, I asked Joye and Alan yesterday and they
 17 assured me that Keith would present. I have
 18 not seen any overheads yet?"
 19 Then Chirgwin sent you the
 20 overheads. Does that refresh your memory,
 21 that you actually received these?
 22 A. Yeah.
 23 Q. Do you have any reason to
 24 believe that you didn't receive this document?
 25 A. No.

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 2 Q. Let me direct your attention, do
 3 you recall -- the CRRC, that's the Clinical
 4 Regulatory Review Committee. Correct?
 5 A. I don't know the exact acronym,
 6 but something like that, yes.
 7 Q. Were you a member of that
 8 committee?
 9 A. I don't think I was a member of
 10 that as a core member. I was probably called
 11 in on occasion.
 12 Q. Why would you be brought in on
 13 occasion?
 14 A. Well, if there were things
 15 discussed that were related to something I
 16 was responsible for. I mean, I was not
 17 responsible for all of clinical research or
 18 regulatory at Merck.
 19 Q. Were you responsible for any
 20 aspect of Protocol 007?
 21 A. No.
 22 Q. So you don't know why you were
 23 called in?
 24 A. Well, because I was -- I mean,
 25 it wasn't only Protocol 007. Some of the

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 2 people who were running Protocol 007 by that
 3 time probably reported to me and I was, as
 4 you have noted before, on the clinical assay
 5 subteam which is a subteam of the BPC.
 6 Q. So you have expertise in the
 7 area of assays. Correct?
 8 A. Yes.
 9 Q. Let me direct your attention to
 10 slide 3 at 561365. And here talks of "Mumps
 11 Expiry Background Chronology of Events." Here
 12 it says, "1997 Clarification that labeled
 13 potencies must reflect end of shelf life claim
 14 (not minimal release)."
 15 Do you see that?
 16 A. Yes.
 17 Q. Does that refresh your memory
 18 that in 1997 is when that clarification
 19 occurred for mumps --
 20 A. Yeah. I mean, that's what it
 21 states here. I mentioned that several times,
 22 that I didn't know anymore when it occurred
 23 but that that particular clarification and
 24 the ensuing discussions ultimately led to the
 25 Protocol 007, not the modeling on stability

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 2 that you referred to later.
 3 Q. So it's your understanding that
 4 as of 1997, CBER required that Merck's end of
 5 expiry shelf life have a minimum of what was
 6 identified in the label at that point, not
 7 just release. Correct?
 8 A. I think that was the first time
 9 when CBER formally informed Merck that that
 10 was how their understanding of the labels had
 11 evolved. And then there was a discussion
 12 ensuing so that it wasn't a one-time event as
 13 far as I remember. But, yes, at that point
 14 in time CBER apparently shared its change of
 15 view.
 16 Q. If you look on the next page,
 17 September 1999 "Chronology of Events Mumps
 18 Overfill." It says, Ongoing CBER concerns
 19 about misbranding result in general -- in
 20 agreement to increase the minimum release spec
 21 for mumps from 4.3 to 5.0. Do you see that?
 22 A. Yes.
 23 Q. If you look on the next page,
 24 "Concerns about Stability," in August of 2000
 25 "Concerns raised regarding compliance with

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 2 stability monitoring during FDA inspection."
 3 Do you see that?
 4 A. Yes.
 5 Q. Do you recall the inspection
 6 that occurred in August of 2000 regarding
 7 mumps stability?
 8 A. No. Only some of the
 9 discussions afterwards that you just shared
 10 with me again.
 11 Q. Do you recall there being a
 12 concern that Merck's then current product was
 13 out of specification with its end expiry
 14 claims?
 15 A. No, I don't recall that until
 16 the dates when you showed me the --
 17 Q. If you see at the bottom it says
 18 December of 2000. The "Expiry trial sera
 19 began to be assayed; validations studies
 20 conducted in parallel." Do you see that?
 21 A. Uh-huh.
 22 Q. So while they were analyzing the
 23 Protocol 007 data, they were at the same time
 24 validating those same studies?
 25 MR. SANGIAMO: Object to the

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 2 form.
 3 THE WITNESS: I'm not sure what
 4 that exactly refers to, what was
 5 validated, whether it was the assay or
 6 something else. You have to see that
 7 this was obviously an ongoing
 8 discussion with CBER and there may
 9 have been very specific CBER requests
 10 that were honored by Merck. And that
 11 would supersede whatever normal
 12 procedure Merck had in place.
 13 BY MR. KELLER:
 14 Q. Is that typical for validating
 15 studies, to have them be validated
 16 concurrently with the running of the study?
 17 A. It depends on -- it depends on
 18 the phase in which the study is done and what
 19 its purpose is. Very typical for Phase I and
 20 Phase 2 studies.
 21 Q. This was Phase 3 study, though,
 22 correct, Protocol 007?
 23 A. No, it's not. No, it's not.
 24 This was not. This was probably a Phase 4
 25 study or a Phase 5 study. It was something

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 2 that was negotiated with CBER. CBER knew
 3 very well what assays were available and were
 4 not available and what had to be developed
 5 because they even influenced which assays had
 6 to be selected.
 7 Q. So is it your testimony that you
 8 knew -- that CBER -- is it your testimony that
 9 CBER knew that Merck was validating the assay
 10 while it was conducting it?
 11 A. That, I don't know. I simply
 12 wouldn't know. But it is my testimony that
 13 CBER had a major role in deciding on this IgG
 14 assay that you mentioned earlier.
 15 Q. Why do you say that?
 16 A. Because it came out of CBER.
 17 It was CBER who suggested that assay in the
 18 first place.
 19 Q. How do you know they suggested
 20 it?
 21 A. That was what I always heard.
 22 Q. Who did you hear that from?
 23 A. Probably from CBER as well as
 24 from Merck people. I don't remember who
 25 specifically told me. But this is an ongoing

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2 discussion. It was an ongoing discussion.

3 Q. What was the ongoing discussion?

4 A. I don't know the details

5 anymore. Just what I remember is that this

6 particular assay format was suggested by CBER.

7 Q. Do you know whether or not Merck

8 had brought it up to CBER first and asked if

9 they could use it?

10 A. No, I don't know that.

11 Q. Do you know whether or not CBER

12 required that to use the rabbit anti-IgG, that

13 it would have to properly validate that assay

14 before it was used?

15 A. You'd have to ask Kathy Carbone

16 since she would know that better than I. I

17 don't know.

18 Q. Let me direct your attention to

19 slide 6 which is the chronology of events for

20 preliminary results of expiry trial. Do you

21 see that?

22 A. Yes.

23 Q. Here it says February '01,

24 "Subset analysis indicates that 4.0 log (but

25 not 3.7...) dose will likely be acceptable."

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2 Do you see that?

3 A. Yes.

4 Q. Then in March it says, "Subset

5 analysis results included in response to FDA

6 warning letter regarding compliance with

7 expiry potency claim."

8 Do you see that?

9 A. Yes.

10 Q. So is it fair to say that Merck

11 was using the preliminary subset analysis as

12 proof that the vaccine worked below 4.3 log at

13 end expiry?

14 MR. SANGIAMO: Object to the

15 form.

16 THE WITNESS: I think that's an

17 over interpretation. I think in

18 discussions with CBER at the time

19 Merck agreed to provide whatever data

20 were available, and CBER probably

21 asked to provide any data that were

22 available. So Merck provided the

23 data.

24 BY MR. KELLER:

25 Q. Do you know that for a fact or

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2 are you just --

3 A. No.

4 Q. -- summarizing?

5 A. Well, I -- it was mentioned in

6 some of the mails that you showed me.

7 Q. But you don't recall. Let me --

8 do you recall any discussion that Merck used

9 the results of Protocol 007's PRN assay to

10 prevent CBER from recalling the product that

11 was out on the market below 4.3 end expiry?

12 A. I do not.

13 Q. You don't know. If you look on

14 the last date in this chronology, December

15 '01, "CBER indicates that compliance concerns

16 may preclude using the mumps PRN data."

17 Do you see that?

18 A. Yes, I see that.

19 Q. Do you know what the compliance

20 concerns were?

21 A. Vaguely. I remember that there

22 was an FDA inspection of the lab that ran the

23 assay as opposed to manufacturing. And then

24 that in that particular -- I wasn't in the

25 lab so I can't tell you all the details, but

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2 there seemed to be compliance concerns

3 primary around documentation of the results,

4 whether they were signed off and whether they

5 had the right format and so on. Which is not

6 atypical for a research laboratory. That may

7 be what CBER says here, but I can't speak for

8 CBER.

9 Q. Were you involved at all in

10 responding to CBER with regard to those

11 compliance issues?

12 A. No. Certainly not directly

13 because I wasn't in the lab. I didn't even

14 know what the exact compliance issues were.

15 Q. Do you recall there being any

16 issues about Merck retesting samples without

17 written justification?

18 A. Not specifically, no.

19 Q. Let me direct your attention to

20 slide 10 of this presentation that was made to

21 the clinical regulatory review committee on

22 January 22, 2002.

23 MR. SANGIAMO: I'm going to

24 object to the preamble.

25 BY MR. KELLER:

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2 Q. It says, "Current Status."

3 A. Wait, wait, wait, wait. Wait a

4 second. What's this here? This is -- this

5 is -- okay. That's the presentation. Okay.

6 So you're just referring to that presentation

7 which was likely presented at the CRRC.

8 Q. Yes. Do you have any reason to

9 believe that it wasn't presented at that

10 meeting?

11 A. Well, no. I don't have any

12 reason to believe that a presentation wasn't

13 presented at that meeting, but this is the

14 attachment of the e-mail that came with the

15 invitation which you gave me. So is it

16 exactly the same presentation that was given

17 or not, I don't know, I would expect it to

18 be.

19 Q. It's the one that you got,

20 though. Correct?

21 A. It's the one I got. I'm just

22 objecting to the additional premises that I

23 know what was actually presented there and

24 can reconstruct it out of my memory 15 years

25 later.

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2 Q. But you have no reason to

3 believe that it wasn't provided?

4 A. No, I have no reason to believe

5 anything.

6 Q. Sure. If you look at slide 10

7 under "Current Status," it says, Response to

8 CBER comments on mumps PRN assay submitted

9 January 21, 2002.

10 In the third bullet point it

11 says, "Products still not compliant with

12 labeled mumps potency 95% lower bound of

13 potencies through end of shelf life is 4.0

14 log.

15 "However, subset analysis

16 suggests that 4.0 log (but not 3.7 log) mumps

17 dose will likely be acceptable."

18 Each time a log tests below 4.3,

19 MMD must file a Biologic Product Deviation

20 Report to CBER detailing results of

21 investigation and medical impact (estimate

22 around 6 to 10 a year).

23 Do you see that?

24 A. Yes.

25 Q. Were you involved at all in MMD

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2 filing BPDR reports to CBER?

3 A. No. Unless they contained

4 clinical data and they would have asked me

5 for clinical data. But not in the filing at

6 all.

7 Q. Do you know if Merck ever

8 submitted a BPDR for those 106 lots?

9 A. No.

10 Q. You don't know, okay.

11 Can you see the last -- on

12 page -- on slide 14, "Mumps Expiry Issue Path

13 Forward?"

14 "Strategies for ensuring

15 compliance if expiry trial data cannot be

16 used."

17 Do you see that?

18 A. Yes.

19 Q. Do you recall any discussion at

20 Merck regarding the failure of Protocol 007's

21 PRN assay reaching the conclusions that were

22 required as part of the end points?

23 MR. SANGIAMO: Object to the

24 form.

25 THE WITNESS: The only thing I

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2 remember was what is listed here on

3 the slide that we looked at before

4 where -- that CBER indicated that

5 there might be compliance issues. I

6 don't know what they are and I can't

7 speculate what exactly they were. And

8 then the fallback would have been to

9 use the ELISA.

10 BY MR. KELLER:

11 Q. And so the path forward here, do

12 you recall any discussion about the path

13 forward -- let me strike that.

14 The term "path forward," is that

15 a term used at Merck that you've seen in the

16 past?

17 A. I've seen it used in many

18 places, yes. Including Merck.

19 Q. What does that mean to you?

20 A. Something that goes in a

21 direction in time probably. Instead of

22 backward.

23 Q. So it's projecting the future,

24 how to get to a future result. Correct?

25 A. Probably, yes.

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 2 Q. And here number 2 it says,
 3 "Reduce 90% lower bound for stability losses."
 4 Do you have any idea what they're talking
 5 about there?
 6 A. No. That's a manufacturing
 7 issue. I wouldn't be involved in the
 8 discussions of how they ran their stability
 9 models.
 10 Q. Do you recall any discussion
 11 about the next statement, "Reduce shelf-life
 12 to 13 months - not considered feasible"?
 13 A. No.
 14 Q. Do you recall any discussion at
 15 Merck that it's one log loss projections from
 16 its then current stability model projected
 17 that the shelf life would be below 12 months?
 18 A. Not specifically, no. I
 19 remember what you showed me, that there was a
 20 model anyway that predicted potential one log
 21 losses, but I don't remember a discussion of
 22 a shorter shelf life.
 23 Q. Do you recall any discussion
 24 about one log loss converted to a shelf life
 25 of 12 months or lower?

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 2 A. No.
 3 Q. Do you --
 4 MR. SANGIAMO: I think he
 5 answered, Jeff.
 6 THE WITNESS: I said no.
 7 BY MR. KELLER:
 8 Q. I'm sorry.
 9 A. Was too simple an answer. You
 10 don't take no?
 11 Q. No, yeses are all fine.
 12 Here it says, "Increase in
 13 release titer - safety concerns." Is there
 14 here a discussion -- do you recall a
 15 discussion about increasing the overfill in
 16 order to improve?
 17 A. Where do you have that here?
 18 Q. Number 2.
 19 A. In a theoretical way I do not
 20 specifically, but I would certainly have been
 21 one who would have objected to doing that
 22 without data.
 23 Q. I see. Why would you have
 24 objected to that without data?
 25 A. Well, you can't just fill in

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 2 more mumps virus or any other live virus for
 3 that matter, if you don't have data to
 4 support that it's a --
 5 Q. What kind of data would you look
 6 at?
 7 A. Well, that's the difficulty.
 8 You would be particularly -- you would be
 9 particularly concerned about the very rare
 10 events like aseptic meningitis and that --
 11 this particular mumps vaccine does not have
 12 associated with it, which is the reason it's
 13 used in the United States as opposed to the
 14 virology strains. But those events are so
 15 rare that they cannot be practically measured
 16 and that's where the feasibility comes in. I
 17 don't know whether they were -- I mean, you
 18 know, that's only on the safety side.
 19 Q. Were you involved at all with
 20 the prior overfill where they increased the
 21 amount of mumps they put into every virus in
 22 1999?
 23 A. I don't really -- in 1991?
 24 Q. 1999.
 25 A. 1999.

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 2 Q. The overfill.
 3 A. No, I don't remember that.
 4 Also 1999 I wasn't at Merck, so I wouldn't
 5 have been either informed or involved.
 6 Q. Here it says, "Improvement in
 7 stabilizer (urea)." Do you see that?
 8 A. Yes.
 9 Q. Do you recall any discussion
 10 about actually changing the MMR II product by
 11 changing the stabilizer in it to help improve
 12 its stability over 24 months?
 13 A. Well, I don't remember any
 14 discussions in this particular context. I
 15 remember them in very different context with
 16 the WHO but not necessarily even led by
 17 Merck. So I -- for this purpose, no, I don't
 18 remember it.
 19 Q. Do you recall -- and the last
 20 one says, "Improvement in assay variability --
 21 limited room for further improvement."
 22 Do you see that?
 23 A. Yes.
 24 Q. That's talking about the
 25 stability model. Correct?

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 2 MR. SANGIAMO: Object to the
 3 form.
 4 THE WITNESS: I don't know. You
 5 expect me to speculate, but I think
 6 it's probably, I think, to the
 7 stability model.
 8 BY MR. KELLER:
 9 Q. Do you recall any discussion
 10 about Merck trying to improve the assay
 11 variability of its stability model?
 12 A. No, I don't, but I think that's
 13 a logical thing that one would consider.
 14 Q. I'm sorry?
 15 A. It's a logical thing to
 16 consider, but I don't remember any specific
 17 discussion. Mind you this is manufacturing
 18 so it wouldn't be my --
 19 Q. Sure. Let me have you turn to
 20 the next page at 16, and it's "GMP Compliance
 21 Issues Recounting of Test Wells." What does
 22 GMP mean?
 23 A. Good manufacturing practice.
 24 Q. Under "Background" in the second
 25 bullet point says, Spreadsheet developed

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 2 during preliminary -- during testing and
 3 preliminary subset included flags for
 4 statistical and operational acceptance
 5 criteria triggered recounts and retests.
 6 Do you see that?
 7 A. Uh-huh.
 8 Q. Do you recall any discussion --
 9 you talked about generally that there was a
 10 compliance issue in the lab. This retesting,
 11 do you know whether or not Merck actually went
 12 back and retested vaccine failures?
 13 A. No, I do not.
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: I do not. What I
 17 remember is what I told you, that
 18 there were documentation issues. But
 19 that was pretty general. I don't
 20 remember the details.
 21 BY MR. KELLER:
 22 Q. You don't know if they followed
 23 your suggestion of retesting the vaccine
 24 failures?
 25 MR. SANGIAMO: Objection.

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 2 THE WITNESS: It wasn't actually
 3 a suggestion. It was I was expressing
 4 what kind of data I would like to see
 5 as a clinician.
 6 BY MR. KELLER:
 7 Q. I see. Here it says under
 8 "Concerns," "Recounts were made, dated, and
 9 signed, but not justified, on the raw data
 10 sheets."
 11 Do you see that?
 12 A. Yes.
 13 Q. Do you recall any discussion at
 14 Merck regarding the justification for changing
 15 data without -- changing data without
 16 justification?
 17 A. It doesn't say here that data
 18 were changed. All it says is that the
 19 recounts were made. That doesn't mean that
 20 any data was changed. It just means that the
 21 same plaques were counted again and it was
 22 probably dated and signed and recorded. So
 23 it doesn't change data. It just counts them
 24 again.
 25 Q. You don't recall any discussion

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 2 about data being changed?
 3 A. No.
 4 Q. Here it says the "Rules
 5 developed/implemented after starting to assay
 6 the expiry trial sera."
 7 Do you see that?
 8 A. I see that.
 9 Q. What do you understand that to
 10 mean?
 11 A. Well, I don't know what rules
 12 it applies to. Maybe rules on recounts or
 13 rules on other things, documentations. So it
 14 doesn't really mean much if I tell you what I
 15 think of it because it depends on what it is.
 16 Q. Sure. Let's go to the next
 17 page, "Impact of Recounts." Here it says on
 18 the first bullet point, "Majority of recounts
 19 involved pre-vaccination sero which were
 20 positive at one dilution only."
 21 Do you see that?
 22 A. Uh-huh.
 23 Q. Do you understand what that
 24 means?
 25 A. Well, I can read the sentence,

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2 but I don't know whether that is just because

3 of how the sera they recounted happened to

4 be, whether it was a choice. I didn't even

5 know that there was a recount, so leave alone

6 whether the --

7 Q. Can you think of any clinical --

8 MR. SANGIAMO: Jeff.

9 THE WITNESS: Leave alone

10 whether there was any deliberate

11 selection.

12 BY MR. KELLER:

13 Q. I see. Can you think of any

14 reason to recount only one data set that's

15 one -- that's positive one dilution?

16 MR. SANGIAMO: Objection.

17 THE WITNESS: I can think of

18 reasons to recount any data set. If

19 you see a valid reason why it might

20 have been counted wrongly, you recount

21 it.

22 BY MR. KELLER:

23 Q. Would you recount all data or do

24 you just recount a certain subset of data?

25 MR. SANGIAMO: Objection.

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2 THE WITNESS: In general it

3 depends on what the error is. So in

4 principle I would probably recount all

5 data if they were all the same. If,

6 however, there are something -- there

7 are something -- some specific

8 characteristics, for example, that

9 something is particularly hard to see

10 or you're not worried about the ones

11 that are in the middle of a

12 distribution but you may be worried

13 about the ones -- if you have a dish

14 that's full of plaques, if you get too

15 many points, they're hard to count.

16 If you have too little, they're may be

17 hard to recognize. So there may be

18 reasons why something recounted

19 because the error is higher. But I

20 don't know what the case here is.

21 BY MR. KELLER:

22 Q. Here it says, "Recounts showed

23 that plaques had been missed." So they added

24 more plaques. Is that correct?

25 MR. SANGIAMO: Objection.

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2 THE WITNESS: No, that's

3 incorrect. If the statement says that

4 they had been missed, it means that --

5 not that they were added, but that

6 they hadn't been seen before. It

7 means in the first count you see maybe

8 ten plaques and you let somebody look

9 again and they find 15 plaques.

10 BY MR. KELLER:

11 Q. So if they're only finding

12 plaques that had been missed, that's one

13 direction. Correct?

14 A. No. It's one direction on that

15 specific plate, but it's not necessarily one

16 direction in the assay, because it may move

17 them in either direction depending on what

18 the dilution is that you test. It's not

19 unidirectional in terms of outcome, it's only

20 unidirectional in terms of the physical

21 measuring object that you have.

22 Q. But if it was unidirectional as

23 to outcome, would that cause you concern?

24 MR. SANGIAMO: Objection.

25 THE WITNESS: Potentially. But

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2 that's not what is described here.

3 Obviously if you look at any -- if you

4 look at a measure for which you have

5 more likelihood of making an error,

6 you would be more likely to repeat it

7 because your measure is not as good.

8 BY MR. KELLER:

9 Q. In the next bullet point says,

10 "Recounts resulted in pre-vaccination sero

11 becoming negative and therefore valid for

12 inclusion in pre-protocol analysis (subjects

13 included in analysis increased from 449 to

14 514)."

15 Do you see that?

16 A. Yeah.

17 Q. So by changing -- recounting

18 these specific results at one dilution, missed

19 plaques were recounted and had the result

20 of -- for just the pre-positives, converting

21 pre-positives to pre-negatives 65 of these

22 samples. Is that fair statement there?

23 MR. SANGIAMO: Object to the

24 form.

25 THE WITNESS: Well, that's what

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
2 it seems to say here.
3 BY MR. KELLER:
4 Q. So if the results of recounting
5 appear to occur in one direction and change
6 results, would that cause you to have concern
7 with how the assay was conducted?
8 A. Not necessarily. It depends on
9 again what it's due to. I mean, something
10 that's hard to see you would miss more often
11 than something that's easy to see. If you
12 have titers of several hundreds, you know
13 that the blades are black, doesn't matter
14 whether they're 449 or 451.
15 Q. I see. So in this case we're
16 talking about --
17 A. Then you have to look -- when
18 you talk about impact, you have to look at
19 does that really change the result, not just
20 the classification.
21 Q. Well, pre-positives mean that
22 those kids are not included in the assay,
23 correct, for the plaque reduction
24 neutralization assay?
25 A. They're not included in --

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
2 they're included in the assay, but they're
3 not counted as seroconverters. So you have
4 to look at the end -- when you compare the
5 end results with corrected and uncorrected
6 results, whether there is any impact on this
7 correction in terms of the outcome.
8 Otherwise, you're talking about something
9 which is not very useful.
10 Q. Do you recall any discussion at
11 Merck regarding the impact of rabbit anti-IgG
12 had on the plaque reduction neutralization
13 assay in that it increased the pre-positives
14 as well as increased the seroconvert --
15 A. No.
16 Q. -- for neutralize the pre --
17 strike that.
18 Do you recall any discussion at
19 Merck regarding the use of rabbit anti-IgG in
20 the plaque reduction neutralizing assay in
21 Protocol 007 that had an impact on the
22 pre-positives, that increased the number of
23 pre-positives?
24 A. No, I don't. I mean, as I said
25 before, I don't even specifically remember

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
2 discussing adding the rabbit IgG at all leave
3 alone its impacts.
4 Now would be a really good time
5 to take another break.
6 Q. Sure.
7 A. I'm sorry, but I'm getting
8 older.
9 Q. That's fine.
10 VIDEOGRAPHER: Off the record
11 3:10. This will end disc number four.
12 - - -
13 (A recess was taken.)
14 - - -
15 VIDEOGRAPHER: Back on the
16 record at 3:17. Beginning of disc
17 number five.
18 MR. KELLER: I'd like to mark as
19 Exhibit 11.
20 - - -
21 (Exhibit Schodel-11, 10/19/01
22 Letter, Bates MRK-KRA01469018 -
23 01469020, was marked for identification.)
24 - - -
25 BY MR. KELLER:

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
2 Q. Exhibit 11 is a document that
3 bears Bates stamp number 1469018 through 020.
4 And it's a document dated October 19, 2001,
5 from Manal Morsy to Henrietta Ukwu regarding
6 CBER teleconference (October 16, 2001):
7 Mumps -- Measles, Mumps and Rubella ELISAs.
8 I'll say, Dr. Schodel, you are identified on
9 the cc as well as identified as participating
10 in this meeting with CBER on this date. Can
11 you tell me -- if you can take a minute to
12 look at this document and tell me if you
13 recall participating in this teleconference, I
14 mean this meeting on -- this teleconference on
15 October 16, 2001?
16 A. Okay.
17 Q. Do you recall participating in
18 this teleconference?
19 A. Honestly I don't, but I read --
20 I glanced over the meeting minutes.
21 Q. Do you have any reason to
22 believe that you didn't attend this meeting?
23 A. No.
24 Q. Do you have any reason to
25 believe that these meeting minutes are not

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 accurate?
 3 A. No.
 4 Q. Were these meeting minutes
 5 generated by Merck in its ordinary course of
 6 its business?
 7 A. I suspect so.
 8 Q. Do you know whether or not these
 9 meeting minutes would be provided to CBER?
 10 A. They would be.
 11 Q. If you look at this teleconference
 12 that occurred on October 16, 2001 --
 13 A. 19. You've got 16.
 14 Q. The date of this memo is three
 15 days later. It identifies the CBER
 16 participants as Kathy Carbone, Dr. Steven
 17 Rubin, Dr. Henry Hsu and Dr. -- I mean, and
 18 Ms. Luba Vujcic. Do you see that?
 19 A. Uh-huh.
 20 Q. Those were the folks that were
 21 typically working on the Protocol 007 assays
 22 at CBER, the primary contacts for Merck?
 23 A. I don't know who else was
 24 working on that particular protocol, but
 25 certainly I've seen their names in

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 association with the protocol.
 3 Q. Let me have you turn your
 4 attention to page 2, 1469019 under "Summary of
 5 discussion." Under the "Wild type mumps ELISA
 6 cutoff."
 7 Do you see that?
 8 A. Yes.
 9 Q. That's the ELISA arm of Protocol
 10 007. Correct?
 11 A. Well, that's the assay used in
 12 Protocol 007, but it is also -- the
 13 discussion here is about not so much only
 14 Protocol 007 but whether the ELISA cutoff was
 15 set right apparently.
 16 Q. Because that was going to be
 17 used with respect for gaining approval of
 18 ProQuad, too. Correct?
 19 A. That's correct.
 20 Q. So if you look in the second
 21 bullet point on 1469019 it says, "Assay
 22 variability and true seroconversion around the
 23 cutoff."
 24 CBER requested clarification on
 25 how we would be able to distinction between a

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 true difference of two samples measuring 9 and
 3 10 Ab ELISA units and the inherent variability
 4 of the assay. CBER reminded Merck of their
 5 position regarding a threshold versus a 4 fold
 6 increase for Varicella gpELISA where a 4 fold
 7 rise is required for assignment of
 8 seroconversion (i.e. less than equal to 1.25
 9 pre to greater than equal 5 post).
 10 Do you see that?
 11 A. I see that.
 12 Q. So that exact or that very
 13 similar example that's being raised at this
 14 meeting had already been discussed internally
 15 at Merck --
 16 MR. SANGIAMO: Objection.
 17 BY MR. KELLER:
 18 Q. -- in Exhibit 9. Do you
 19 remember that?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: Well, it's --
 23 you're making assumptions here. It's
 24 not the exact same issue. It's the
 25 same approach of requiring in addition

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 to a seroprotection cutoff, also a
 3 fourfold rise criterion. But it's not
 4 the same assay, it's not the same
 5 variability and it's not the same
 6 numbers.
 7 BY MR. KELLER:
 8 Q. So there's -- at this point CBER
 9 is still considering whether or not it was
 10 going to require Merck to do a fold increase
 11 to set the serostatus cutoff for its ELISA
 12 assay. Correct?
 13 A. That is correct.
 14 Q. If you look on the next page, in
 15 the middle -- one, two, three, four, five
 16 bullet points -- five paragraphs down it says,
 17 "It should be noted that if the question about
 18 justification and relevance of the mumps ELISA
 19 cutoff could be addressed (i.e. by correlating
 20 to PRN), then a 4 fold criterion would not be
 21 necessary. If, however there continues to be
 22 uncertainty about the biological/clinical
 23 relevance of the cutoff, it is expected that
 24 CBER would require a 4 fold...criterion, as
 25 that would be necessary to demonstrate

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2 significant response to the vaccine. This

3 reasoning would parallel that which is used

4 for measles and rubella ELISAs. CBER did not

5 require a fold rise in these assays because

6 measles and rubella ELISAs employ a recognized

7 reference standard for seroprotection."

8 Do you see that?

9 A. Yes.

10 Q. So is it fair to say that if

11 Merck did not correlate its PRN assay to its

12 ELISA assay to justify its static cutoff, it

13 was going to be required to do a fourfold

14 criterion?

15 MR. SANGIAMO: Objection. Calls

16 for speculation.

17 THE WITNESS: I think that's

18 speculation. The -- that's the fear

19 expressed by the person who wrote

20 this, but that is not what CBER has

21 stated.

22 BY MR. KELLER:

23 Q. Isn't this sent to CBER?

24 A. It is sent to CBER but it does

25 not reflect only CBER's position. It

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 reflects a discussion.

3 Q. I see. So --

4 A. It was not sent to us by CBER

5 saying this is what you have to do. This is

6 what will happen if you don't do it. So this

7 is a lot of speculation that you're asking me

8 for.

9 Q. Sorry. This is a discussion

10 that Merck had with CBER where CBER was

11 communicating what it expected, though.

12 Correct?

13 A. Yes, but the criteria are -- so

14 CBER expected additional information which

15 was provided. And it also recognized that

16 there are constraints in the assay. It also

17 recognized that in other assays like rubella

18 and measles, this kind of a criterion was not

19 applied.

20 Q. Because there there was some

21 reference standard for seroprotection at that

22 serostatus cutoff. Correct?

23 A. That is correct. But not the

24 only reason because the same argument that

25 you made before that if something is variable

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 right around that cutoff could be applied for

3 these as well regardless of whether there is

4 a correlation or not.

5 Q. Why would CBER -- what was the

6 discussion in this meeting that CBER was

7 requesting that Merck correlate that

8 serostatus cutoff to the PRN?

9 A. I don't speculate on CBER's

10 intent.

11 Q. You understood that's what CBER

12 was asking for?

13 A. It was one of the issues they

14 requested, and that was -- it was up to CBER

15 to request it without justifying it.

16 Q. I see. Did Merck correlate its

17 serostatus cutoff to the PRN assay?

18 A. Since CBER requested it, they

19 would have probably done it.

20 Q. Did you ever see that data?

21 A. I don't remember it in detail,

22 but I may have seen it.

23 Q. Do you know whether or not that

24 was ever submitted? You don't know if it was

25 ever submitted to CBER?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 A. No, I don't know that.

3 Q. But you do know that the

4 fourfold criteria was not required for

5 purposes of the wild-type ELISA that was used

6 and not just Protocol 007 but used for

7 approval of ProQuad's BLA?

8 A. I do know that.

9 Q. They didn't require the fourfold

10 criteria?

11 A. No, they did not. But the

12 reason why they did not may be different.

13 There are other -- if you read through the

14 whole document, you find, for example, it is

15 actually -- it turns out that the ELISA is

16 more conservative in assigning seropositivity

17 and seronegativity. So CBER may have had

18 other reasons than simply the correlation for

19 allowing the ELISA to go forward with a

20 fourfold -- without a fourfold rise.

21 MR. KELLER: Can I get that

22 answer back? I'm sorry.

23 - - -

24 (The court reporter read the

25 pertinent part of the record.)

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 - - -
 3 BY MR. KELLER:
 4 Q. What would those reasons have
 5 been?
 6 A. They're listed in here somewhere.
 7 MR. SANGIAMO: Object to that
 8 question as calling for speculation.
 9 BY MR. KELLER:
 10 Q. You can answer.
 11 A. I can't speculate on what CBER
 12 wanted, but the assay -- let me see where it
 13 was. I just read something here. Actually
 14 it speaks directly to what CBER said, so I
 15 don't have to speculate. You can actually
 16 read what CBER said. It's the last paragraph
 17 on the second page. It says, "CBER pointed
 18 out that a correlation rate of 92% was low,
 19 particularly when related to the expected
 20 criteria for success in terms of
 21 seroconversion rate (5% delta, 90% floor),
 22 but noted that the ELISA seemed to be more
 23 conservative than the PRN in assignment of
 24 low sero-positives."
 25 So that was CBER's opinion.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 And that is obviously a major factor in
 3 making a decision. And they stated it here.
 4 So that's not a speculation, it's -- you have
 5 it in writing here.
 6 Q. So your statement is that PRN
 7 assay was more variable at assigning low
 8 seropositives?
 9 A. The PRN assay was probably more
 10 variable full stop as PRN assays are known to
 11 be.
 12 Q. I see.
 13 A. And it goes on also as stated
 14 by CBER, "It was pointed out to CBER that
 15 although this was true for pre-vaccination
 16 samples, results of this limited data set
 17 show that in case of post-vaccination sera,
 18 the ELISA was more sensitive than the PRN in
 19 assigning high titers," which also helps in
 20 the distinction.
 21 Q. But taking all that together,
 22 CBER wanted to see some sort of correlation
 23 between the PRN assay and the serostatus
 24 cutoff because of the wild-type ELISA.
 25 Correct?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. No. CBER wanted to see some
 3 type of correlation going into that meeting.
 4 Taking all that together, I don't want to
 5 speculate, but reading what CBER said, I'm
 6 not so sure that they were as interested
 7 anymore.
 8 Q. I see. Let's find out.
 9 A. And they still wanted it to be
 10 shown. Whether the data mattered, I don't
 11 want to speculate on that.
 12 Q. I see. But they wanted to see
 13 that data?
 14 A. Obviously.
 15 MR. KELLER: Let me mark as
 16 Exhibit 12.
 17 - - -
 18 (Exhibit Schodel-12, 4/25/02
 19 E-mail with attachment, Bates
 20 MRK-KRA00544512 - 00544538, 00544540 -
 21 00544543, was marked for identification.)
 22 - - -
 23 BY MR. KELLER:
 24 Q. For the record, Exhibit 12 is a
 25 document that bears Bates stamp number 544296

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 through --
 3 MR. SANGIAMO: That's not what
 4 you gave us. Wrong one.
 5 - - -
 6 (A discussion off the record
 7 occurred.)
 8 - - -
 9 MR. KELLER: I'm sorry. Just
 10 mark this one the next one. Mark this
 11 one as 13.
 12 - - -
 13 (Exhibit Schodel-13, 5/7/02
 14 E-mail with attachment, Bates
 15 MRK-KRA00544296 - 00544324, was marked
 16 for identification.)
 17 - - -
 18 THE WITNESS: Disregard 12 at
 19 this point.
 20 BY MR. KELLER:
 21 Q. Just set it aside for now.
 22 Start with 13. Let me mark Exhibit 13 Bates
 23 number 544296 through 331836. Wait. Whoa
 24 whoa, whoa. Sorry. It's hard to get good
 25 help these days. Let me strike that.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Let me mark Exhibit 13 Bates
 3 number 544296 through 544324. And for the
 4 record, Exhibit 13 is a document, an e-mail
 5 from Keith Chirgwin to Dr. Schodel regarding
 6 draft document mumps cutoff, and attaches a
 7 series of exhibits. This e-mail is dated
 8 May 7, 2002. And if you could take a look at
 9 this for a minute, Doctor, and tell me, if you
 10 recall receiving this e-mail.
 11 A. I don't recall receiving this
 12 specific e-mail, but I mean, it's along the
 13 same lines.
 14 Q. Do you have any reason to
 15 believe you didn't receive it?
 16 A. No.
 17 Q. Any reason to believe you didn't
 18 receive the attachments to it?
 19 A. No.
 20 Q. In this e-mail from Mr. -- from
 21 Dr. Chirgwin he writes, Florian, This is the
 22 latest version of the mumps cutoff CBER
 23 response from Joe. As per the previous e-mail
 24 message, it appears that things have gotten
 25 stuck with regard to the table that Joe

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 presented at the VAC several weeks ago showing
 3 the breakdown by ELISA strata of the
 4 discordant PRN negative/ELISA positive sera.
 5 Do you see that?
 6 A. Yes.
 7 Q. That's the vaccine assay
 8 committee. Correct?
 9 A. Uh-huh.
 10 Q. That's the committee that you
 11 were either the co-chair or a member?
 12 A. Yes.
 13 Q. It goes on to say that the large
 14 majority of these discordants had ELISA titers
 15 less than 40 and one concern is that
 16 presenting the data in this fashion may prompt
 17 CBER to request that the ELISA cutoff be
 18 raised.
 19 Do you see that?
 20 A. Yes.
 21 Q. Do you recall discussions
 22 regarding the removal of certain tables in
 23 response to CBER regarding the cutoff that
 24 there was a concern that that data would lead
 25 CBER to increase the cutoff?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. No.
 3 Q. If you look further, Chirgwin
 4 says, "I agree that CBER did not specifically
 5 indicate that we would be required to
 6 demonstrate concordance. However in reviewing
 7 the meeting minutes from last October
 8 (attached below), it is...clear that they are
 9 going to look closely at how sera with values
 10 around the cutoff are classified in the two
 11 assays."
 12 Do you see that?
 13 A. Yes.
 14 Q. In this October, do you believe
 15 that's referring back to that October 16,
 16 2001, meeting or teleconference where the
 17 serostatus cutoff was discussed?
 18 A. I assume so.
 19 Q. At least -- and he goes on to
 20 say, "At least based on October's discussion,
 21 if we are unable to provide sufficient
 22 reassurance about the clinical relevance of
 23 the ELISA cutoff (which in Kathy's mind means
 24 linking this to the PRN) then we may end up
 25 with some type of a fold-rise criterion which

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 I assume we would rather avoid if possible."
 3 Do you see that?
 4 A. Yes.
 5 Q. So there was a concern that if
 6 Merck provided CBER certain data, that they
 7 would increase the ELISA cutoff. Is that what
 8 this document is saying?
 9 A. That's what it seems to say
 10 here.
 11 Q. So Joe, that's Joe Antonello,
 12 correct, he's a statistician?
 13 A. I assume that if it's not Joe
 14 Heyse, it must be Joe Antonello.
 15 Q. See below that there's a
 16 reference, it says, "Joe I removed tables 6 c
 17 and 6 d and information referring to them from
 18 the 007 ELISA and PRN comparison document
 19 (Attachment 2)...," and he says, "...too
 20 distracting." Do you see that?
 21 A. Yes.
 22 Q. Let me have you draw attention
 23 to Exhibit 12 that we had just marked
 24 previously. On the e-mail on 544512, there's
 25 a couple documents attached to it. And

<p style="text-align: right;">Page 310</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 Attachment 1 on 55 -- 544514 is a -- the</p> <p>3 Table 6c and 6d that the previous -- or the --</p> <p>4 that was identified as being removed. Have</p> <p>5 you ever seen this table before?</p> <p>6 MR. SANGIAMO: Object to your</p> <p>7 preamble. What is your question,</p> <p>8 whether he has seen the table at</p> <p>9 544514?</p> <p>10 MR. KELLER: Yes.</p> <p>11 MR. SANGIAMO: Okay.</p> <p>12 THE WITNESS: I would have</p> <p>13 probably seen it as an attachment of</p> <p>14 this e-mail provided -- I mean,</p> <p>15 provided I read the details of all</p> <p>16 these e-mails because I was not the</p> <p>17 primary person responsible anymore.</p> <p>18 BY MR. KELLER:</p> <p>19 Q. You see that you were cc'd on</p> <p>20 this e-mail.</p> <p>21 A. Yeah. I was cc'd on a lot of</p> <p>22 e-mail, 200 or 300 a day.</p> <p>23 Q. This was sent to Joseph</p> <p>24 Antonello. Do you see that?</p> <p>25 A. Yes.</p>	<p style="text-align: right;">Page 312</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 number of discrepant paired sera in ELISA and</p> <p>3 PRN relative to what is expected per assay</p> <p>4 variability in the STD range."</p> <p>5 Do you see that?</p> <p>6 A. Yes.</p> <p>7 Q. STD, is that standard deviation?</p> <p>8 Do you understand that to be standard</p> <p>9 deviation?</p> <p>10 A. I'm not exactly sure what STD</p> <p>11 stands for here.</p> <p>12 Q. Do you have any reason to</p> <p>13 believe that you didn't receive this e-mail?</p> <p>14 A. No. Just, you know, I'm copied</p> <p>15 as are others.</p> <p>16 Q. Sure. It goes on to say, "I</p> <p>17 understand that at 1 STD and 2 STD</p> <p>18 discrepancies observed fall within expected %</p> <p>19 but at 3STD we have more discrepancies than</p> <p>20 what can be explained by just assay</p> <p>21 variability...."</p> <p>22 Do you see that?</p> <p>23 A. Yes.</p> <p>24 Q. Do you understand why that would</p> <p>25 be important?</p>
<p style="text-align: right;">Page 311</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 Q. And Jonathan Hartzel?</p> <p>3 A. Yes, yes, yes.</p> <p>4 Q. And David Krah?</p> <p>5 A. Yeah.</p> <p>6 Q. And Alan Shaw? Those were the</p> <p>7 folks that were working on Protocol 007.</p> <p>8 Correct?</p> <p>9 A. Dave was working in Alan's lab,</p> <p>10 yes.</p> <p>11 Q. And Alan reported to Emimi?</p> <p>12 A. Yes.</p> <p>13 Q. And David Krah reported to</p> <p>14 Emimi?</p> <p>15 A. To Alan Shaw.</p> <p>16 Q. And here Manal Morsy, she was</p> <p>17 the regulatory liaison at this time frame,</p> <p>18 wasn't she?</p> <p>19 A. I believe so, yes.</p> <p>20 Q. And here she writes Joe, Jon,</p> <p>21 Luwy, Alan and Dave:</p> <p>22 "Please review the documents</p> <p>23 attached - two sections are needed (marked in</p> <p>24 red in the document).</p> <p>25 "Joe: a table showing the</p>	<p style="text-align: right;">Page 313</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 MR. SANGIAMO: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: No.</p> <p>5 BY MR. KELLER:</p> <p>6 Q. It goes on to say, "Joe, also</p> <p>7 please confirm that the attachments enclosed</p> <p>8 are in fact the audited documents (I have</p> <p>9 deleted as you know tables 6c and 6d and their</p> <p>10 corresponding text from attachment 2 - I have</p> <p>11 attached the tables and text deleted for your</p> <p>12 reference - which I would like to replace as</p> <p>13 we discussed with a table showing</p> <p>14 discrepancies within std ranges instead of</p> <p>15 cutoffs)...."</p> <p>16 Do you see that?</p> <p>17 A. Uh-huh.</p> <p>18 Q. So if you look on 544514, table</p> <p>19 6c and 6d, is this a 4-by-4 table that you</p> <p>20 discussed earlier?</p> <p>21 A. It's a little bit of a</p> <p>22 different format. But it's a classification</p> <p>23 of subsets by titer in another assay, I</p> <p>24 guess.</p> <p>25 Q. Is this identifying the false</p>

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 positives?
 3 A. Quite frankly, I don't remember
 4 what HN stands for anymore.
 5 Q. HN is the plaque reduction
 6 neutralization assay done in Protocol 007?
 7 A. That's what I thought, but I
 8 just wanted to make sure. Yeah, it's a
 9 listing of numbers. I find these listings
 10 not very helpful because the cells, the
 11 individual cells become relatively small and
 12 so the inferences you can draw from them are
 13 very limited.
 14 Q. So when Chirgwin said that we
 15 didn't want to give these tables to CBER
 16 because they may raise the serostatus cutoff
 17 in the wild-type ELISA, what about these
 18 tables would indicate that this would suggest
 19 that the serostatus cutoff that was proposed
 20 at ten should be raised?
 21 MR. SANGIAMO: Again, I object
 22 to the preamble of your question.
 23 THE WITNESS: I can't speculate
 24 on what Keith might have thought. I
 25 look at these tables differently as

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 indicating absolutely nothing.
 3 BY MR. KELLER:
 4 Q. So when it says --
 5 A. That's why it shouldn't have
 6 been communicated, because they're
 7 meaningless and they're fine, they appear to
 8 say something but they don't really.
 9 Q. I see. So when it says 60, when
 10 it's looking at titers between 10 and 20, 20
 11 and 40 and 40 and 80 and identifying the
 12 numbers, the subset of negative samples in the
 13 PRN versus all samples, the number on
 14 percentage, that's identifying a -- discordant
 15 results that were positive. Correct?
 16 A. Well, it seems to be identifying
 17 a percentage of titers that would be positive
 18 by ELISA or positive by neut and negative by
 19 the other assay. But it's always very small
 20 numbers.
 21 Q. I see. Wasn't CBER concerned
 22 about the discordant results around the
 23 cutoff?
 24 A. You have to ask CBER that.
 25 Q. So you can't sit here today and

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 tell me how -- why this -- these two tables,
 3 if provided to CBER, may lead them to increase
 4 the cutoff as identified by Keith Chirgwin?
 5 A. No, I personally don't think
 6 that that would be the case because if they
 7 interpret them the way I do, then they would
 8 say, okay, at a lower titer, the likelihood
 9 is that the standard deviation of the assay
 10 is higher and the likelihood for a
 11 discordance between two different assays is
 12 also higher. That doesn't mean that the
 13 assays are not concordant. It just means
 14 that you always see the discordance show up
 15 at the extremes.
 16 Q. I see. Was there any discussion
 17 about any kind of standard that CBER was
 18 looking for with respect to what percentage of
 19 false positives it would deem acceptable in
 20 this concordance analysis?
 21 A. You're assuming here two
 22 things. First of all, that there was a
 23 standard. The answer is no. Secondly, that
 24 these are false positives in one assay or the
 25 other. The concordance just means that

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 they're differently interpreted in the
 3 different assays. It doesn't mean that one
 4 is false and the other one is wrong. What
 5 CBER would also consider is what assay is
 6 more robust, more reliable, and in which
 7 direction does it classify the samples. And
 8 as you have seen from the CBER's -- from
 9 CBER's previous comment, they noted that
 10 actually the ELISA was more conservative.
 11 Q. I see. But when you compared
 12 the two assays, which it appears that Kathy
 13 Carbone was asking about in terms of relying
 14 upon a serostatus cutoff versus requiring some
 15 fourfold increase, she wanted Merck to compare
 16 around the cutoff. And so if I'm reading this
 17 document correctly, a cutoff between 10 and 20
 18 would result in 24 percent false positive
 19 rate, a cutoff between 20 and 40 would reduce
 20 that false positive rate to 11.8 percent. Is
 21 that correct?
 22 A. No, that's an assumption based
 23 on a very small number. And, therefore, you
 24 cannot infer that as a general statement.
 25 You can just say that in this particular

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 2 classification, one assay classified a
 3 certain proportion into one direction and the
 4 other assay in the other direction. You
 5 can't make -- from such a small sample you
 6 can't make such a general statement.
 7 May I just come back to your
 8 intro? Kathy Carbone is a person, I don't
 9 know what she was thinking and what she
 10 wanted. You are referring this to me through
 11 an e-mail from Keith Chirgwin who is specific
 12 as to what Kathy Carbone -- maybe he knows
 13 what Kathy Carbone wants. Neither is Kathy
 14 Carbone CBER nor am I, Keith Chirgwin, nor do
 15 I know what Kathy Carbone was thinking.
 16 Q. You're talking -- you're stating
 17 that this is a small sample. This represents
 18 all the ELISA assays?
 19 A. Still remains a small sample.
 20 Q. I see. So these percentages,
 21 these are the discordant percentages. Correct?
 22 A. Well, in this subset of
 23 available samples at the time.
 24 Q. And so another way of saying
 25 that are false positive rate. Correct?

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 2 A. The false positive rate always
 3 assumes that one of them is the truth and the
 4 other one is not.
 5 Q. So if you look at the top of
 6 this chart, "A further analysis of the
 7 post-vaccination titers is provided in Tables
 8 6c and 6d. Table 6d shows the frequency
 9 distribution of AIGENT titers for (a) all
 10 AIGENT positive post-vaccination samples, and
 11 (b) the subset of ELISA negative in AIGENT
 12 positive post-vaccination samples." Then it
 13 goes to "...relative distribution of Table c
 14 indicate that" -- let me go back to this. Let
 15 me strike that.
 16 Do you recall any discussion at
 17 Merck that CBER was concerned that the
 18 discordant false positive rate be below a
 19 certain percentage?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: Beyond what I just
 23 read in this e-mail, no.
 24 BY MR. KELLER:
 25 Q. Is it fair to say that based on

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 2 the data that's on this chart, that a titer at
 3 40 or above would have had a false positive
 4 rate of 3.4 percent based on this chart?
 5 A. Yes, that would be wrong.
 6 Q. Why is that wrong?
 7 A. Because you're extrapolating
 8 from a small band 40 to 50 -- 40 to 80,
 9 sorry, to the whole behavior and you see that
 10 it actually changes and that the sample size
 11 gets larger, too.
 12 Q. So when it says 20 -- titer 20
 13 to 40 and it says percentage 11.8 percent,
 14 again, you're saying that's not a false
 15 positive rate for that range?
 16 A. It's a rate of discordance
 17 between the two assays.
 18 Q. I see.
 19 A. At that particular very narrow
 20 bandwidth.
 21 Q. I see.
 22 A. In this particular sample which
 23 may not apply to any other sample.
 24 Q. So your testimony is that this
 25 analysis has no relevance to whether or not

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 2 the serostatus cutoff is correct at 10?
 3 A. It shows -- it shows how the
 4 two assays, so the answer is no. It shows
 5 that the two assays show a certain
 6 discordance and that the discordance is
 7 larger around the cutoff, as you would
 8 expect. But it does not necessarily imply
 9 that one cutoff is better than the other. In
 10 fact, the other part that CBER noted is that
 11 using the 10 cutoff in the ELISA moves you in
 12 a more conservative direction.
 13 Q. So is it fair to say from this
 14 chart, that as you raise the cutoff, the
 15 discordant results go down?
 16 A. That's fair. So you make a
 17 very reliable assay more concordant with a
 18 very unreliable assay.
 19 Q. So is it fair to say that the
 20 discordant results, if you increase the titer
 21 from 10 to a range of 10 to 20, would go from
 22 24 percent to a range of 20 to 40 down to
 23 11.8 percent?
 24 A. No, that's a -- that is --
 25 you're extrapolating too much and generalizing

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 2 from a distribution in a small sample size.
 3 Q. I see.
 4 A. You would have to build a
 5 confidence interval around that. If you
 6 think of it in terms of a confidence
 7 interval, it could be much wider.
 8 Q. So as you sit here today,
 9 Dr. Schodel, it's your testimony that you have
 10 no idea why Keith Chirgwin was concerned that
 11 by providing these tables to CBER, that they
 12 would increase the serostatus cutoff?
 13 MR. SANGIAMO: Object to the
 14 form.
 15 THE WITNESS: I don't know what
 16 Keith was thinking, but I don't share
 17 his concern.
 18 BY MR. KELLER:
 19 Q. I'm sorry, did you review the
 20 draft response that was going to go to CBER
 21 with respect to this justification for the
 22 serostatus cutoff?
 23 A. I don't know. I mean, I had --
 24 you know, I had Luwy in there who was a very
 25 good clinical monitor, and I generally relied

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 2 on my people doing work. So I don't know
 3 whether I reviewed it in detail.
 4 Q. Who would be the one that was
 5 responsible for signing off on the response to
 6 CBER with respect to this issue of serostatus
 7 cutoff?
 8 A. That's an interesting question
 9 that I can't answer, because probably --
 10 again, I'm speculating. Probably Keith
 11 Chirgwin and the lab, but I'm not sure.
 12 Q. It wasn't you?
 13 A. Oh, certainly not.
 14 Q. And it wasn't Dr. Musey?
 15 A. Not directly. He's responsible
 16 for the clinical data in there.
 17 Q. So if you look at 544515 which
 18 is this draft response to Merck regarding --
 19 A. Which one is that, the next one
 20 or --
 21 Q. It's Exhibit 544515.
 22 MR. SANGIAMO: Still within 12.
 23 BY MR. KELLER:
 24 Q. Still in Exhibit 12.
 25 A. Okay.

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 2 Q. Here's a draft, and I'll
 3 represent to you that this ultimately became
 4 086 for the record. Under 1 on the first page
 5 it says, "CBER request that Merck provide
 6 additional justification for the cutoff
 7 chosen for the Mumps" --
 8 A. Where are we now, I'm not
 9 following you?
 10 Q. The first page.
 11 MR. SANGIAMO: We're on this
 12 document. Jeff, do you intend to give
 13 him a chance to read this --
 14 MR. KELLER: No, I'm just going
 15 to go through --
 16 MR. SANGIAMO: -- two-page
 17 document?
 18 MR. KELLER: The topics are very
 19 general.
 20 MR. SANGIAMO: Are you going to
 21 ask him questions about it?
 22 THE WITNESS: If you're going to
 23 ask me questions, let me read it,
 24 otherwise I'm not going to answer your
 25 question.

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 2 BY MR. KELLER:
 3 Q. Take all the time you need to
 4 read it if that's what you need to do for me
 5 to ask you if you recall seeing this document?
 6 MR. SANGIAMO: Is that the only
 7 question, whether he recalls seeing
 8 it?
 9 MR. KELLER: I have some other
 10 questions.
 11 MR. SANGIAMO: Well, then he
 12 needs to read it.
 13 BY MR. KELLER:
 14 Q. Go ahead, you can read it. It's
 15 a two-page document. Go ahead.
 16 A. This document I have is much
 17 longer.
 18 Q. The cover letter.
 19 A. So you just want me to
 20 concentrate on the cover letter here, not on
 21 the -- not on where it --
 22 Q. We'll get there in a minute. If
 23 you want to read the attached response, go
 24 ahead.
 25 MR. SANGIAMO: Jeff, is it your

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 2 representation that this is the
 3 document that was submitted to CBER?
 4 MR. KELLER: It's a draft.
 5 MR. SANGIAMO: It's a draft,
 6 okay. I thought you said it was a
 7 document that was submitted.
 8 MR. KELLER: I said for the
 9 record this draft is what was
 10 submitted as 086.
 11 THE WITNESS: Excuse me, I
 12 didn't hear that last one. The
 13 ultimate one submitted was different
 14 from this one?
 15 BY MR. KELLER:
 16 Q. I'm asking if this is the one
 17 that was submitted to you, if you reviewed it?
 18 Let me know when you're ready, sir.
 19 A. There's obviously -- there's
 20 still questions in there and so...
 21 Q. It's a draft.
 22 A. Okay.
 23 Q. If you look on the cover letter,
 24 the draft cover letter to CBER under "With
 25 focus on the following issues," it says, CBER

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 2 requests that Merck provide additional
 3 justification for the cutoff chosen for the
 4 Mumps wild-type ELISA comparing the ELISA
 5 cutoff to the AIGENT assay cutoff and
 6 specifically to provide.
 7 Do you see that?
 8 A. Uh-huh.
 9 Q. And so the attached -- the next
 10 page under B, "Identification of individual
 11 titers in relative range around cutoffs of
 12 both assays in order to confirm that both
 13 assay are characterizing sera in a comparable
 14 fashion."
 15 Do you see that?
 16 A. Yes.
 17 Q. Then Merck attaches its response.
 18 Correct?
 19 MR. SANGIAMO: Object to the
 20 form.
 21 BY MR. KELLER:
 22 Q. This is a draft response?
 23 A. I don't know whether this was
 24 sent to the agency, but this is a draft of
 25 what would have eventually been sent to the

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 2 agency.
 3 Q. I just want to turn your
 4 attention just to the conclusion that's drawn
 5 in this draft at 544524. I understand it's a
 6 draft. Here it says, Conclusion: There is
 7 good agreement between the Mumps wild-type
 8 ELISA and the AIGENT assays in terms of
 9 serostatus classification when using a cutoff
 10 of 10 units in the Mumps wild-type ELISA and a
 11 cutoff of 1 to 32 in the AIGENT assay.
 12 Do you see that?
 13 A. Yes.
 14 Q. What -- is there a scientific
 15 term for good agreement? What does good
 16 agreement mean? Let me strike that.
 17 What does good agreement mean in
 18 the context of this analysis, if you know?
 19 A. I don't know a specific number,
 20 but apparently they showed the degree of
 21 agreement, and it looked reasonably high, and
 22 so they called it a good agreement.
 23 Q. And so the discordant results
 24 that were in charts 6c and 6d that had
 25 24 percent discordant results for a serostatus

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 2 cutoff between 10 and 20, and that went down
 3 to 11.4 percent with a serostatus cutoff from
 4 20 to 40, that was considered a good
 5 agreement?
 6 A. You're extracting an
 7 inappropriate comparison that is based on
 8 small numbers and just a subfraction of the
 9 total results. If you look at Table 8 here,
 10 for example, you see the expected percentages
 11 of misclassified samples by the assays
 12 standard deviations from the cutoff, that
 13 gives you a better measure of what would be
 14 expected and what would be observed.
 15 Q. So what standard deviation -- I
 16 mean, you have zero to three. Right?
 17 A. Yes.
 18 Q. And so in the previous e-mail,
 19 in the e-mail that attaches this document,
 20 there's a discussion here that at three
 21 standard deviations we have more discrepancies
 22 than that can be explained by just assay
 23 variability. That seemed to be a big issue
 24 to --
 25 A. Joan Staub who was not --

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 2 MR. SANGIAMO: You have to let
 3 Mr. Keller finish his question.
 4 MR. KELLER: Let him answer.
 5 MR. SANGIAMO: No, no, no.
 6 That's a big issue, what's the rest?
 7 To and then what comes after that?
 8 MR. KELLER: Can you read back
 9 my question?
 10 - - -
 11 (The court reporter read the
 12 pertinent part of the record.)
 13 - - -
 14 BY MR. KELLER:
 15 Q. -- to Manal Morsy, the
 16 regulatory liaison.
 17 So my question is, three
 18 standard deviation, is your testimony that
 19 that's not significant?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: I didn't say that.
 23 But what I said is that she may not
 24 have looked at the complete analysis
 25 that is presented here in this draft

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 2 and that may be further enhanced in
 3 the ultimate -- what was ultimately
 4 sent because I'm not sure that the
 5 analyses were even complete here. So
 6 you're showing me something that at
 7 the time was not completed.
 8 What I was starting to point out
 9 to you is that it's quite normal to
 10 see that as you get closer to the
 11 cutoff and no standard deviations, you
 12 would expect to see a higher mismatch.
 13 At no standard deviation it's 50/50,
 14 and then it goes up. And so I'm not
 15 clear to -- it's not clear to me that
 16 based on the analysis I see here in
 17 this draft Manal's concern is valid.
 18 MR. KELLER: Let me mark as
 19 Exhibit 14.
 20 - - -
 21 (Exhibit Schodel-14, E-mail
 22 chain with attachments, Bates
 23 MRK-KRA00561199 - 00561209, was marked
 24 for identification.)
 25 - - -

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 BY MR. KELLER:
 3 Q. Exhibit 14 is a document that
 4 bears Bates stamp number 561199 through
 5 561209. This is a series of e-mails and two
 6 attachments. And if you look at the first
 7 e-mail that's sent from Manal Morsy to Keith
 8 Chirgwin and you, Dr. Schodel, on May 31,
 9 2002, can you tell me, do you recall seeing
 10 this e-mail?
 11 A. I don't recall seeing this
 12 specific e-mail, but if I read it, I can
 13 probably figure out what it means.
 14 Q. Sure.
 15 A. Okay. I haven't read this
 16 attachment yet.
 17 Q. We're not even going to look at
 18 the attachment. So let's just talk about the
 19 e-mails.
 20 In here Dr. Manal -- I'm sorry.
 21 Dr. Morsy sent you and Dr. Chirgwin an e-mail
 22 and cc'd Joe Antonello, Dr. Antonello and
 23 Dr. Hartzel, Dr. Schofield. Is Schofield a
 24 doctor?
 25 A. Schofield.

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 2 Q. Schofield. Is he a doctor?
 3 A. Yes, he is. I think anyway.
 4 Q. And here Manal Morsy is saying,
 5 "The attached is completed based on...", this
 6 is on 561200 which is her May 31, 2002,
 7 e-mail, "The attached is completed based on
 8 feedback and edits received and incorporated
 9 today (unless Keith, Florian..., that's you,
 10 Dr. Schodel, "...or Tim send in comments
 11 before noon tomorrow Friday)." It goes on, "I
 12 plan to finalize for submission early next
 13 week pending auditing sign off for attachments
 14 2 and 3 (attachment 2 was I believe previously
 15 audited but is modified by deletion of
 16 Tables 6c, 6d and associated text)."
 17 Do you see that?
 18 A. Uh-huh.
 19 Q. So that table that we went
 20 through earlier has been deleted from what was
 21 to be submitted to CBER?
 22 A. Yeah, but read further down.
 23 Q. I will.
 24 A. The information is still --
 25 Q. Yes. Joe - I removed Tables 6c

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 2 and 6d and associated text you re-inserted in
 3 attachment 2 to avoid confusions since Table
 4 6d has different ELISA titer grouping used to
 5 show number of discrepancies between the
 6 AIGENT and the ELISA within each group than
 7 what we -- you have -- than which you have
 8 used in attachment 2 -- Table 2 of
 9 attachment 3, (titer groups in the deleted
 10 Table 6d are ELISA titers of 10 to 20, 20 to
 11 40, and 40 to 60, et cetera, whereas they are
 12 based on sd from cutoff in table -- in
 13 attachment 3 and so are grouped differently:
 14 ELISA titer groups of 1sd (10 to 14), 2sd (14
 15 to 20), 3sd (20 to 28) et cetera).
 16 Do you see that?
 17 A. Uh-huh.
 18 MR. SANGIAMO: I just want to
 19 note for the record, there were a
 20 couple of points where you didn't read
 21 the right word but we can go back to
 22 the document as need be.
 23 MR. KELLER: Sure.
 24 BY MR. KELLER:
 25 Q. So here Joe Antonello, the

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 2 biostatistician working on this analysis
 3 between the PRN assay and the wild-type ELISA
 4 assay who wanted to insert these two tables in
 5 the way that it was presented, it was removed
 6 by Manal Morsy, the liaison, FDA liaison
 7 because she thought it may encourage CBER to
 8 increase the cutoff, and so she had them
 9 replaced with a different way of identifying
 10 that data from using groups of cutoffs to
 11 using groups of standard deviations. Is that
 12 a fair statement?
 13 MR. SANGIAMO: Object to the
 14 form.
 15 THE WITNESS: There's too much
 16 speculation in there. She had removed
 17 the tables because, as I read it, the
 18 information is adequately captured in
 19 the alternative table and actually
 20 better understandable.
 21 BY MR. KELLER:
 22 Q. I see. And so why didn't they
 23 just put it in both tables?
 24 MR. SANGIAMO: Object to form.
 25 Calls for speculation.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 THE WITNESS: Why would you
 3 submit -- why would you submit
 4 redundant information to CBER and make
 5 it hard for them to interpret it?
 6 BY MR. KELLER:
 7 Q. Well, evidently is it fair to
 8 say that Mr. Antonello, this biostatistician,
 9 wanted that data in here?
 10 MR. SANGIAMO: Object to the
 11 form. Calls for speculation.
 12 THE WITNESS: I don't know that
 13 for sure. He may not have noted that
 14 he's already provided the same
 15 information on another table as well.
 16 BY MR. KELLER:
 17 Q. He evidently re-inserted it
 18 after Manal Morsy took it out in the last
 19 draft.
 20 A. I can't speculate.
 21 MR. SANGIAMO: Object to the
 22 form.
 23 BY MR. KELLER:
 24 Q. You can't speculate. I see. So
 25 Manal Morsy goes on to say, "I understand that

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 2 you have a desire to include them but you have
 3 very nicely captured all the discrepancy
 4 information and how it is distributed relative
 5 to the ELISA 10 cutoff in table 2 of
 6 attachment 3 so the information in the end is
 7 included, reflected accurately and completely
 8 to CBER and that's what's critical and
 9 important."
 10 Do you see that?
 11 A. Yes.
 12 Q. But it's just included in the
 13 different format that the biostatistician
 14 didn't agree to. Correct?
 15 A. No.
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: You're speculating.
 19 BY MR. KELLER:
 20 Q. I see.
 21 A. We don't say that -- she
 22 doesn't say that he didn't agree to it. She
 23 just -- I mean, we often have people who
 24 provide a data dump. They generate all kinds
 25 of tables. And at the end, you have to make

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 2 a call. It's her call because she's the
 3 regulatory liaison to figure out which ones
 4 are more useful.
 5 Q. I see. So then she goes on,
 6 "Please review to insure that no statements
 7 were accidentally left behind in attachment 2
 8 that are specific to these two tables."
 9 So she's pretty adamant about
 10 removing his description of what was in those
 11 tables from what was provided to CBER. Is
 12 that a fair assessment?
 13 A. No, not as far as the
 14 description goes. In fact, she makes extra
 15 sure that no statements are in there that
 16 would wrongly refer to the tables, not to the
 17 now attached whatever number two was. Just a
 18 matter of editing the document at the end to
 19 make sure that whatever statement is in there
 20 is accurate.
 21 Q. I see. And so -- okay.
 22 MR. KELLER: Let me mark as
 23 Exhibit 15.
 24 THE WITNESS: May I just point
 25 out to you that actually the content

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 2 of these tables is in the document,
 3 here in this draft, 3a and 3b.
 4 BY MR. KELLER:
 5 Q. Where is the content of that
 6 information in these documents?
 7 A. The tables that you were
 8 particularly asking about seem to be Tables
 9 3a and 3b here.
 10 Q. Do you know whether or not this
 11 was provided to CBER?
 12 A. Do you know whether it was
 13 provided to CBER? I don't.
 14 MR. SANGIAMO: Doctor, you just
 15 have to answer his question.
 16 BY MR. KELLER:
 17 Q. I do.
 18 A. While you're looking, I'll take
 19 another short break. Is that okay?
 20 Q. Sure.
 21 VIDEOGRAPHER: Off the record at
 22 4:15. This ends disc number five.
 23 - - -
 24 (A recess was taken.)
 25 - - -

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 2 VIDEOGRAPHER: Back on the
 3 record at 4:21. The beginning of disc
 4 number five -- six.
 5 MR. KELLER: Let me mark as the
 6 next exhibit, Exhibit 15 which had
 7 previously been marked with -- by
 8 Fisher Exhibit 17.
 9 - - -
 10 (Exhibit Schodel-15, E-mail
 11 chain, Bates MRK-KRA00791315 -
 12 00791319, was marked for identification.)
 13 - - -
 14 BY MR. KELLER:
 15 Q. Nor the record, Exhibit 15 is a
 16 document bearing Bates stamp number 791315
 17 through 19 which is a series of e-mails.
 18 Doctor, I'd like to direct your
 19 attention to the last e-mail on page 791319.
 20 This is an e-mail from Joe Antonello to Keith
 21 Chirgwin, and you're cc'd on this. The
 22 subject is Comparing Mumps wild-type ELISA and
 23 AIGENT Assay, June 29, 2004. If you want to
 24 take a minute to review that.
 25 A. Okay.

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 2 Q. Here this is an e-mail -- and
 3 Keith -- Joe was saying, writing to Keith, "In
 4 response to your MVX...", that's a voicemail
 5 system that Merck had at the time. Correct?
 6 A. Yes.
 7 Q. So he got a -- this appears to
 8 be a voicemail from Keith Chirgwin who he's
 9 responding to. In the middle of the page it
 10 says, In that response, we contended that
 11 there was reasonably good agreement between
 12 the two assays in terms of serostatus
 13 classification when using a cutoff of 10 Ab
 14 units in Mumps wild-type and a cutoff of 1 to
 15 32 in the AIGENT assay, so I am concerned when
 16 you say that the two assays are discordant
 17 around the cutoff. Concluding that the two
 18 assays agree reasonably well was important for
 19 the purpose of arguing that the ELISA was
 20 acceptable substitute for the neutralizing
 21 assay.
 22 Do you see that?
 23 A. Yes.
 24 Q. Does that lead you to believe
 25 that Merck is arguing that they have

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2 correlated their plaque reduction

3 neutralization assay to the ELISA assay?

4 A. No, it means exactly what it

5 says, that a serostatus classification

6 concordance testing was done and that the

7 using the cutoffs of 1 of 10 and 1 to 32

8 there was reasonable concordance.

9 Q. And so Merck wanted to use that

10 as a substitute, so to rely upon the ELISA as

11 a substitute for the neutralization assay?

12 A. Those are Joe's words. I don't

13 know what he means with a substitute.

14 Q. I see.

15 A. I mean, there were two assays

16 used in 007. So ultimately the ELISA was

17 important for that particular study and it

18 was also used for the ProQuad filings. So

19 obviously CBER accepted that the ELISA was a

20 reasonable assay to measure mumps activity.

21 Q. I see. Here he says, "I do

22 agree with your key points..., " and he's

23 responding to the Keith Chirgwin, "We don't

24 really know what a clinically protective level

25 is in either assay...."

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2 Do you see that?

3 A. Yes.

4 Q. He's talking both about the

5 wild-type ELISA and Merck's PRN assay as used

6 in Protocol 0097. Correct?

7 A. Probably, yes.

8 Q. Do you agree with that statement?

9 A. Yes.

10 Q. So if you see on the next e-mail

11 on 791318, dated June 29, 2004, later on that

12 evening Chirgwin responds to Dr. Antonello,

13 and you're cc'd on here, Dr. Schodel, "Thanks

14 Joe. Just to clarify, I understand that the

15 PRN and ELISA track fairly well and this is

16 what I conveyed to Steve Rubin. The question

17 is to what degree are these assays

18 concordant."

19 Do you see that?

20 A. Yes.

21 Q. Do you understand what he meant

22 by the term "concordant"?

23 A. No.

24 Q. He goes on and says, He was

25 suggesting specific criteria for concordance

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2 when I am not sure we could meet.

3 And so this is Steve Rubin

4 saying that he wants specific criteria for

5 concordance.

6 His suggestion was that we focus

7 on sera with low antibody titers just above

8 the ELISA cutoff, and that they would like to

9 see no more than 10 percent of such ELISA low

10 positive sera score negative to PRN assay.

11 Do you see that?

12 A. Yes.

13 Q. So isn't that what Table c and

14 Table d identify?

15 MR. SANGIAMO: I'm going to

16 object to your reading of that, not

17 just because there were a couple of

18 mistakes in there, but you also

19 inserted something that was not from

20 the document itself.

21 BY MR. KELLER:

22 Q. I'll rephrase it if you need to.

23 "His suggestion was that we focus on sero with

24 low antibody titers just above the ELISA

25 cutoff, and that they would like to see no

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2 more than 10% of such ELISA low positive sero

3 score negative in the PRN."

4 Do you see that?

5 A. Yes, I see that.

6 Q. Isn't that exactly what Table c

7 and Table d were identifying?

8 A. No. It overlaps with that

9 statement, but it's not exactly the same.

10 Q. I see. How does it overlap?

11 A. Well, it overlaps by showing in

12 a selected small sample how the low antibody

13 titers just above the ELISA cutoff are scored

14 in the PRN.

15 Q. Then he goes on and says, I do

16 not recall whether we ever did such a subset

17 analysis with low positives - this seems like

18 a problematic approach as the low percentage

19 of "false-positive" would depend on which

20 specific sera are selected for inclusion in

21 such an analysis.

22 Do you see that?

23 A. Yes.

24 Q. So this term "false-positive,"

25 what do you understand that to mean?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Well, I understand that to mean
 3 that they saw something -- a different result
 4 in one of the assays than in the other assay
 5 which does not -- doesn't speak to absolute
 6 truth or falseness. It just simply speaks to
 7 the level of discordance or concordance.
 8 Q. Let's go to the first page of
 9 this e-mail. Here Michael Dekleva -- who is
 10 Michael Dekleva?
 11 A. Mike at the time, he was at
 12 some point regulatory and clinical. And
 13 before that I think he was quality assurance
 14 and MMD. So I don't know what he was at that
 15 time.
 16 Q. I see. So he sends you an
 17 e-mail on July 2, 2004, regarding comparing
 18 mumps wild-type ELISA or WT ELISA and AIGENT
 19 assay. You understand it to refer to the
 20 ELISA and PRN assays in Protocol 007?
 21 A. Yes.
 22 Q. Alison and I are pulling it
 23 together. In what we've been able to find so
 24 far, there doesn't seem to be any
 25 documentation that CBER actually concurred

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 with our recommendations regarding the WT
 3 ELISA and choice of less than 10 Ab unit
 4 cutoff. We requested their concurrence, but
 5 never received a response.
 6 It goes on, in order -- In
 7 looking at the old documentation it's clear
 8 that CBER was very interested in the PRN assay
 9 for evaluating persistence. Afterwards we
 10 claimed that there was strong concordance
 11 between the PRN and wild-type ELISA, although
 12 around the cutoff (less than 10 Ab) there's a
 13 greater chance of seeing positive results with
 14 the PRN rather than the ELISA.
 15 Do you see that?
 16 A. Yes.
 17 Q. And so this strong concordance,
 18 is that the analysis that you reviewed earlier
 19 where they were looking at whether or not the
 20 two assays --
 21 A. Yes.
 22 Q. It goes, Perhaps because of that
 23 there were slightly higher seroconversion
 24 rates reported with the wild -- WT ELISA
 25 versus PRN in the 007 study (something like 94

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 versus 92 percent). Then he writes is that
 3 significant with a question mark.
 4 Nonetheless, we opted for use of the wild --
 5 WT ELISA for future studies.
 6 Do you see that?
 7 A. That's how he summarized the
 8 situation, yeah.
 9 Q. And those future studies were
 10 the ones that were done for ProQuad?
 11 MR. SANGIAMO: Objection. Calls
 12 for speculation.
 13 BY MR. KELLER:
 14 Q. Do you understand that's what
 15 he's talking about?
 16 MR. SANGIAMO: Calls for
 17 speculation.
 18 THE WITNESS: I don't know.
 19 BY MR. KELLER:
 20 Q. You don't know. And finally it
 21 goes, "So...we are pulling the information
 22 together, including all prior CBER
 23 communications. It may be that Steve Rubin is
 24 simply 'coming up to speed,' or it could be
 25 that he's trying to understand our rationale

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 for selecting an assay that while more precise
 3 and easier to perform, may overestimate
 4 seroconversion rates relative to their
 5 'preferred' (?) PRN assay."
 6 Do you see that?
 7 A. Yes.
 8 Q. So here -- is Mike Dekleva a
 9 doctor?
 10 A. No.
 11 Q. Here he's saying that the
 12 wild-type ELISA may overestimate
 13 seroconversion rates with -- compared to the
 14 PRN assay. Do you see that?
 15 A. I think he's just speculating.
 16 We actually have just seen data to the
 17 converse.
 18 Q. You don't agree with that?
 19 A. No, I don't agree with that.
 20 Q. It goes on to say, I spoke with
 21 Joe Antonello yesterday, and he re-emphasized
 22 that the decision with the PRN assay was very
 23 poor, and he felt that it was really hard to
 24 say whether the differences in the data sets
 25 were significant - influenced to a great

<p style="text-align: right;">Page 350</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 extent by the variability in the PRN assay --</p> <p>3 PRN data.</p> <p>4 Do you see that?</p> <p>5 A. Yes.</p> <p>6 Q. SO do you agree with Joe</p> <p>7 Antonello that the PRN assay was very poor</p> <p>8 with respect to precision?</p> <p>9 A. It was certainly relatively</p> <p>10 worse than the ELISA which is one of the</p> <p>11 reasons why CBER also preferred the ELISA.</p> <p>12 Q. I see.</p> <p>13 A. It's generally harder to make a</p> <p>14 biological assay like a PRN assay as reliable</p> <p>15 as an ELISA. It's well known in the art.</p> <p>16 Q. So do you agree that the PRN</p> <p>17 assay was very poor?</p> <p>18 A. No, those were Joe's words or</p> <p>19 maybe they're Mike's interpretation of Joe's</p> <p>20 words. I don't think it was very poor, but</p> <p>21 the precision, it's a relative statement. If</p> <p>22 you compare it to the wild-type ELISA, it may</p> <p>23 appear very poor because the ELISA is much</p> <p>24 more reliable.</p> <p>25 Q. Wasn't Merck comparing the</p>	<p style="text-align: right;">Page 352</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 closed out the issue - which allowed us to</p> <p>3 proceed with MMR and PQ studies..."</p> <p>4 A. Where is that?</p> <p>5 Q. The top of this?</p> <p>6 A. Oh, here it is, yeah.</p> <p>7 Q. "...at the time - hope this was</p> <p>8 captured."</p> <p>9 MR. SANGIAMO: Let him read.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Sure. PQ there represents</p> <p>12 ProQuad. Correct?</p> <p>13 A. Yes.</p> <p>14 Q. You say, "Agree with Joe - could</p> <p>15 not overemphasize the weakness of the PRN (50%</p> <p>16 specifies!!!!!!)." </p> <p>17 Do you see that?</p> <p>18 A. Yes, I see that.</p> <p>19 Q. So is it your opinion that the</p> <p>20 PRN assay was weak and only had 50 percent</p> <p>21 specificity?</p> <p>22 A. I think it had its weaknesses.</p> <p>23 The 50 percent is a partial misquote. There</p> <p>24 was not -- as we pointed out earlier, there</p> <p>25 was not a formal specificity analysis</p>
<p style="text-align: right;">Page 351</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 cutoffs of the wild-type ELISA with the PRN</p> <p>3 cutoffs in order to confirm that the cutoff</p> <p>4 used in the ELISA was accurate?</p> <p>5 A. In order to satisfy a CBER</p> <p>6 desire. You cannot measure -- you cannot</p> <p>7 confirm that something is accurate with a lot</p> <p>8 of precision with something that in itself is</p> <p>9 imprecise.</p> <p>10 Q. I see. That's what happened</p> <p>11 with Protocol 007. Correct?</p> <p>12 MR. SANGIAMO: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: That's what</p> <p>15 happened not necessarily specifically</p> <p>16 for Protocol 007. That is what will</p> <p>17 happen every time you use a biological</p> <p>18 assay to try to measure concordance at</p> <p>19 the extremes.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. And so here on July 3rd, the</p> <p>22 next day, 2004, Dr. Schodel, you responded to</p> <p>23 Michael Dekleva. And here you write, "Dear</p> <p>24 Mike, Thanks - I distinctly remember a</p> <p>25 conversation with Kathy Carbone in which we</p>	<p style="text-align: right;">Page 353</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 performed, so I couldn't know what the exact</p> <p>3 specificity was. What I was reacting to was</p> <p>4 that in a very, very small sample, in half of</p> <p>5 the samples some of the titers were reduced</p> <p>6 by unspecific reagents such as measles</p> <p>7 extracts, rubella extracts and Varicella</p> <p>8 extracts that summarized in the validation</p> <p>9 report does not necessarily mean that the</p> <p>10 overall specificity is only 50 percent</p> <p>11 because that wasn't formally analyzed. It</p> <p>12 just means exactly that, that there are other</p> <p>13 factors that contribute to the variability of</p> <p>14 the assay. And, again, didn't matter for 007</p> <p>15 because it was a comparative study.</p> <p>16 Q. Well, Doctor, you seem to be</p> <p>17 very well versed in the definition of</p> <p>18 specificity. So here you write 50 percent</p> <p>19 specificity with six exclamation points. So</p> <p>20 at this time that you wrote this, you agreed</p> <p>21 with Joe that the precision was very poor and</p> <p>22 that you could not overemphasize the weakness</p> <p>23 of the PRN assay. Is that a fair statement?</p> <p>24 A. Yes, but I just explained to</p> <p>25 you that the specificity of 50 percent here</p>

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 does not refer to a specific specificity
 3 analysis as could have been performed that
 4 wasn't performed.
 5 Q. I see.
 6 A. So I don't know what the real
 7 number was. I didn't know at the time.
 8 Q. So the 50 percent specificity
 9 you're talking about is whether or not the
 10 neutralization that occurred in this PRN assay
 11 was the result of mumps -- I mean, measles or
 12 rubella?
 13 A. Not at all. No. What I was
 14 reacting to was a data mentioned in the
 15 summary of the validation report which
 16 essentially states if you reread it, that in
 17 a number of sera, in half of them the titer
 18 could only be reduced by mumps so that half
 19 of them were completely specific. And the
 20 other half, some of the plaque reduction, I
 21 don't even know whether it's the titer, just
 22 the plaque reductions seemed to be reduced by
 23 unspecific reagents. That does not yet mean
 24 that the assay overall has a 50 percent
 25 specificity. I just interpreted that as

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 2 meaning that half is 50 percent. It is a
 3 sloppy expression which I should probably not
 4 have used, but it does not reflect on the
 5 overall specificity, nor does it matter.
 6 Q. So it's your testimony today
 7 when you say specificity, you didn't really
 8 mean specificity?
 9 MR. SANGIAMO: Object to the
 10 form. It's argumentative. He's
 11 already addressed this.
 12 THE WITNESS: My testimony today
 13 is that I just translated four out of
 14 eight with something that doesn't
 15 translate into specificity as 50
 16 percent.
 17 BY MR. KELLER:
 18 Q. So you're talking about with
 19 something in the clinical study report?
 20 A. No, it's in the validation
 21 report for the mumps neutralizing assay.
 22 Q. When did you review that?
 23 A. I must have reviewed it around
 24 that time, but because that question arose
 25 again, I looked it up and that's what it was.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. When did you look it up?
 3 A. I looked it up whenever it was,
 4 Monday.
 5 Q. So you went back and looked up
 6 that on Monday?
 7 A. Because I wanted to know what I
 8 had referred to at the time. I don't -- I'm
 9 sorry, maybe you're perfect, but I don't
 10 remember everything that I said in 2004.
 11 Q. That was after you spoke to your
 12 lawyers. Correct?
 13 A. No, not at all. It was after I
 14 saw this e-mail and they asked me what I
 15 meant.
 16 MR. SANGIAMO: Hold on.
 17 Dr. Schodel, you can't discuss our
 18 conversations.
 19 BY MR. KELLER:
 20 Q. So the validation document that
 21 you reviewed, that was a validation document
 22 for the plaque reduction neutralization assay?
 23 A. Yes.
 24 Q. So it was looking at the
 25 specificity of other agents. What other

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 2 agents was it looking at?
 3 A. It was not testing, formally
 4 testing specificity so I shouldn't have used
 5 that term. But it was using rubella,
 6 Varicella -- rubella, measles and cell
 7 extract, uninfected cell extract.
 8 - - -
 9 (Exhibit Schodel-16, Excerpted
 10 document of Clinical Study Report,
 11 Bates MRK-KRA00001270 - 00001466, was
 12 marked for identification.)
 13 - - -
 14 BY MR. KELLER:
 15 Q. I'm going to mark as Exhibit 16
 16 a document that bears Bates stamp numbers 1270
 17 through 1466. This is an excerpted document
 18 of the entire clinical study report. It
 19 doesn't have all the attachments. But I ask
 20 you if you recognize this as the clinical
 21 study report that was used for Protocol 007
 22 and was submitted to CBER?
 23 A. It looks like it.
 24 Q. Let me direct your attention to
 25 1328 of the clinical study report. What is a

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 2 clinical study report?
 3 A. A clinical study report is a
 4 report on the data generated in a clinical
 5 study.
 6 Q. This is the backup data support,
 7 the label change for Protocol 007 to reduce
 8 the potency from 4.3 to 4.1?
 9 A. That's certainly part of the
 10 information. I suspect it's not all the
 11 information.
 12 Q. There's also a supplemental BLA
 13 that goes -- that this is attached to. Correct?
 14 A. Yeah, probably.
 15 Q. Did you ever review this CSR
 16 before it was submitted?
 17 A. I don't remember. It depends
 18 on the time. I generally reviewed CSRs when
 19 I was responsible for them and didn't when I
 20 wasn't, so I don't remember. I mean, the
 21 direct responsible probably at the time would
 22 have been Luwy or another physician. And I
 23 would not always have reviewed all the
 24 details of a clinical study report. There
 25 were a lot of them.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 MR. KELLER: Let me mark as
 3 Exhibit 17.
 4 - - -
 5 (Exhibit Schodel-17, 10/21/03
 6 Memo, Bates MRK-KRA01638866 -
 7 01639147, was marked for identification.)
 8 - - -
 9 BY MR. KELLER:
 10 Q. Exhibit 17 is a document --
 11 A. That's all you want to know on
 12 16?
 13 Q. We're going to go back to it.
 14 Just keep it in front of you.
 15 A. You want me to read it?
 16 Q. No, I'll show you what to look
 17 at.
 18 So Exhibit 17 is a document that
 19 bears Bates stamp number 1638866 through
 20 1639147. And it's a document dated
 21 October 21, 2003, from Mandie Lyon to
 22 Dr. Schodel and a bunch of other people,
 23 subject: "V205C Protocol 007 Clinical Study
 24 Report for Review 2." And there's handwritten
 25 documents -- handwritten notes on this and it

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 2 seems to appear to be signed by you,
 3 Dr. Schodel. Does this refresh your memory
 4 that you did review it and made comments?
 5 A. It looks like my handwriting
 6 for sure.
 7 Q. Let me direct your attention
 8 back to Exhibit 16 which is the formal CSR and
 9 I will represent to you that was submitted to
 10 CBER, according to Merck. If you go back to
 11 1328 -- let me back up a little bit.
 12 Let me go back to 1325 and start
 13 there. Here under 5.5.4.1.
 14 A. Wait, wait, wait. On 1325 I
 15 have 5.7.3.3.
 16 Q. I apologize, I'm looking --
 17 A. Oh, oh, oh. Okay.
 18 Q. It's the center number, not the
 19 one on the right. It's a different number. I
 20 apologize. Let me know when you're there.
 21 A. I think I'm there.
 22 Q. Here at 5.5.4.1 it says,
 23 "Anti-IgG Enhanced Mumps Plaque Reduction
 24 Neutralization Assay." Do you see that?
 25 A. Yes.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. That's the PRN assay that was
 3 used in Protocol 007. Correct?
 4 A. Yes.
 5 Q. If you look on 1328 there's a
 6 topic of "Specificity." Is this a summary of
 7 the specificity analysis that Merck did on
 8 Protocol 007, the PRN assay?
 9 A. Yes, I think it is. It is here.
 10 Q. Is that what you're relying upon
 11 to say it was only 50 percent specific?
 12 A. As I said, I -- this was a bit
 13 of an overstatement. But what I translated
 14 here was that in that "Absorption with the
 15 mock measles or rubella extract yielded similar
 16 results, whereas absorption with the mumps
 17 extract yielded a further reduction in...3 to
 18 4..." I don't remember whether this is what
 19 I based it on. I think it was more the
 20 statement in the validation report.
 21 Q. I see.
 22 A. So I don't really remember, I
 23 don't remember, but I think that's a little
 24 different statement in the validation report.
 25 It's a little different than the statement

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 2 here.
 3 Q. Fair enough. Let me direct your
 4 attention to page 12 -- to 1462. 1461 and
 5 1462 under title 9 "Discussion."
 6 A. Okay.
 7 Q. Here -- actually let me do this:
 8 Let me direct your attention -- this is under
 9 section 9 "Discussion." What is typically the
 10 discussion section in the clinical study
 11 report, does that discuss the -- what is
 12 that -- the purpose of a discussion section?
 13 A. Well, the purpose of the
 14 discussion section is to discuss any issues
 15 that need further discussion. It could be
 16 the endpoints, it could be the assays, it
 17 could be the selection of the population in
 18 which something was done. It's not a very
 19 narrow definition of that.
 20 Q. Let me direct your attention to
 21 1463 in the last paragraph. Let me know when
 22 you get there.
 23 In this paragraph Merck is
 24 representing to CBER that, The mumps wild-type
 25 ELISA used in this study was shown to

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 2 correlate with the PRN assay, and previous
 3 studies have established a strong correlation
 4 between the development of mumps-specific
 5 neutralizing antibodies and vaccine efficacy.
 6 Therefore, the mumps PRN assay and ELISA
 7 results from this study support the
 8 effectiveness of M-M-R II containing a mumps
 9 virus potency of no more than 4.1 log TCID and
 10 the lowering of the mumps virus end expiry
 11 potency from the currently assigned potency of
 12 4.3 to no less than 4.1 log TCID.
 13 Do you see that?
 14 A. Yes, I see that.
 15 Q. So Merck submitted to CBER that
 16 it correlated its wild-type ELISA assay to its
 17 PRN. Does that surprise you?
 18 A. No, as requested by CBER.
 19 Q. So Merck is representing as part
 20 of the CSR that, in fact, it is correlating
 21 its wild-type ELISA assay to its PRN assay to
 22 support the effectiveness of MMR II?
 23 A. Well, indirectly because the
 24 immunologic comparison between these
 25 different preparations of MMR with different

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 2 mumps potencies have relatively similar
 3 immune responses and, therefore, would
 4 expect -- be expected to protect in a similar
 5 way. The assay is just an adjunct. It's
 6 not -- since there is no correlative
 7 protection in the assay, it just shows that
 8 they're similar.
 9 Q. Well, you testified there's a
 10 difference between the concordance, between a
 11 PRN assay and ELISA assay and a correlation
 12 between the two. Here Merck is representing
 13 that it correlated those two assays, isn't it?
 14 A. I didn't say -- while the
 15 difference is -- the difference I pointed out
 16 was more in how you look at the comparison of
 17 two assays. It doesn't -- I didn't
 18 specifically say that one is worse or better
 19 than the other. It's just how you do things.
 20 But I never said that there was a correlation
 21 between any specific titer or any specific
 22 assay and the prevention of disease.
 23 Q. Are you surprised to see Merck
 24 representing to CBER that it did correlate
 25 those two assays, the PRN and wild-type ELISA?

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 2 A. Well, you already know that
 3 CBER asked that that be done and so, of
 4 course, it was done. Because it was done it
 5 had to be summarized in a clinical study
 6 report.
 7 Q. You understand that the use of
 8 these two assays was to show that the
 9 vaccine -- to support vaccine effectiveness?
 10 A. Among other data, yes.
 11 Q. So vaccine effectiveness means
 12 that the vaccine works in the real world,
 13 correct, based on your definition?
 14 A. That's correct, but that's not
 15 based on the PRN assay result.
 16 Q. So when you agreed with Joe that
 17 the PRN assay that's being used to correlate
 18 to the wild-type ELISA is very poor and could
 19 not overemphasize the weakness of the PRN
 20 assay, you think that's appropriate to submit
 21 to CBER that the wild-type assay was
 22 correlated to the PRN assay?
 23 A. Yes. It's actually only very
 24 weak around this particular definition of a
 25 cutoff. It's not overall very poor. That's

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 2 not what anybody said. And therefore, overall
 3 the correlation is pretty good. Most people
 4 are vaccinated at very high titers and then
 5 it would have an almost perfect correlation.
 6 Q. So if Merck submitted this PRN
 7 assay as support and to be considered as a
 8 surrogate of vaccine effectiveness, would that
 9 cause you concern?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: It's not what
 13 Merck has done as far as I can tell.
 14 BY MR. KELLER:
 15 Q. Let me show you the BSLA -- SBLA
 16 which I'd like to mark as Exhibit 32 -- I'm
 17 sorry, Exhibit 18.
 18 - - -
 19 (Exhibit Schodel-18,
 20 Supplemental Biologics License
 21 Application, Bates MRK-KRA00000032 -
 22 00000139, was marked for identification.)
 23 - - -
 24 BY MR. KELLER:
 25 Q. Exhibit 18 bears Bates stamp

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 2 number 32 through 139. Again, this is a
 3 excerpted document, doesn't have thousands of
 4 pages, it has the supplemental biologics
 5 license application.
 6 Doctor, have you seen this
 7 document before?
 8 A. Probably, but I don't remember.
 9 Q. Let me direct your attention to
 10 Bates number 111.
 11 A. 111?
 12 Q. Yes. Under section 2.5.1.5.3,
 13 Study Endpoints, what is a study endpoint
 14 again, Doctor?
 15 A. It's a measure taken in the
 16 study.
 17 Q. Here it says, The Mumps
 18 neutralizing antibodies were measured
 19 immediately prior to vaccination and 6 weeks
 20 postvaccination using the plaque reduction
 21 neutralization assay. The PRN assay was used
 22 as a priority endpoint because it is a
 23 functional assay that can measure the ability
 24 of vaccine-induced immune response to inhibit
 25 viral replication in vitro, and can,

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 2 therefore, be considered a surrogate for
 3 vaccine effectiveness.
 4 What do you understand surrogate
 5 of vaccine effectiveness to mean, Doctor?
 6 A. I think that's a bit of
 7 a surrogate for vaccine. I mean, it's
 8 supportive data that the vaccine has not
 9 changed in that context of the comparison.
 10 You can use it as vaccine effectiveness
 11 because the vaccine has shown effectiveness.
 12 The immunogenicity to it has not changed and,
 13 therefore, you would expect the same
 14 effectiveness does not mean that it directly
 15 correlates with effective.
 16 Q. I see. But isn't Merck
 17 representing --
 18 A. The surrogate simply means that
 19 you can't measure the original, so it means
 20 it stands in for.
 21 Q. Because you couldn't do an
 22 efficacy study today, that's unethical?
 23 A. That's correct.
 24 Q. So the best assay that you can
 25 use is a surrogate of vaccine effectiveness.

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 2 Correct?
 3 A. Any assay that you can use you
 4 would try to use as a surrogate for vaccine
 5 effectiveness showing that the vaccine hasn't
 6 changed since it's been started to use and
 7 looking at the field effectiveness data that
 8 you constantly get. So it doesn't
 9 necessarily have to be the best. It is what
 10 the best effort that you can make. And in
 11 that regard both ELISA and both the PRN were
 12 used to support that the vaccine had not
 13 changed.
 14 Q. I see. And so you're not
 15 concerned that any assay that you considered
 16 to be -- that you stated you cannot
 17 overemphasize the weakness of this assay, you
 18 agreed with Joe Antonello that it was very
 19 poor with regard to precision is being
 20 represented by Merck to CBER as a surrogate
 21 for vaccine effectiveness?
 22 A. No, that doesn't concern me
 23 because you're taking my statements of its
 24 weakness out of context. It's not weak
 25 across the board. It's very precise in

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2 estimating high titers, for example.

3 Q. It's just weak around the

4 cutoff?

5 A. It's relatively weaker than the

6 ELISA.

7 Q. I see. And Merck in the

8 clinical study report stated that it

9 correlated its wild-type ELISA to its PRN

10 assay. Correct?

11 A. That's correct.

12 Q. Do you know that Merck was able

13 to convince CBER to rely only on wild-type

14 ELISA assays going forward based on this

15 correlation analysis?

16 MR. SANGIAMO: Object to the

17 form.

18 THE WITNESS: That is an

19 assumption that -- you make too many

20 assumptions in your question. Even in

21 the document that you showed me, CBER

22 itself provided other reasons why it

23 would rely on the ELISA and which you

24 have read and we talked about. So I

25 would certainly not support the notion

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2 that CBER accepted that solely on the

3 correlation. That being said, the

4 correlation wasn't all that bad.

5 MR. KELLER: I see. Let's take

6 a break.

7 VIDEOGRAPHER: Off the record at

8 4:56.

9 - - -

10 (A recess was taken.)

11 - - -

12 VIDEOGRAPHER: Back on the

13 record at 5:08.

14 - - -

15 (Exhibit Schodel-19, Article

16 draft, Bates MRK-KRA00032482 -

17 00032519, was marked for identification.)

18 - - -

19 EXAMINATION

20 - - -

21 BY MR. MACORETTA:

22 Q. All right. Good evening,

23 Dr. Schodel. We met earlier. My name is John

24 Macoretta. Mr. Keller had to leave so I'm

25 going to finish up with a few additional

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2 questions this evening.

3 A. Okay, John.

4 Q. I'm going to show you what we

5 just marked as Exhibit 19, which I believe is

6 a draft of an academic article for which you

7 were one of the authors. Correct?

8 A. Yes.

9 Q. Do you remember working on this?

10 A. I saw it at some point and I

11 made some comments on it, yes.

12 Q. So you were not the principal

13 drafter, I take it?

14 A. No.

15 Q. Who was?

16 A. I suspect it was Tim Schofield,

17 but I don't really know.

18 Q. Who is the first person -- the

19 first author is C. Marchant. Who is that?

20 A. I don't know.

21 Q. Not a Merck employee I take it.

22 Right?

23 A. I really don't know. I don't

24 know. I don't know.

25 Q. Okay. Fair enough. I want to

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2 talk to you towards the end, if you go towards

3 the end, the Bates numbered page ending in

4 517.

5 A. 517. Okay.

6 Q. If you see at the top there's a

7 sentence that's highlighted with a comment, it

8 says, "Comment (FS12)." Take a look at that

9 comment.

10 A. Yeah, I can't read this, it's

11 too small print.

12 Q. I don't know how to help you

13 with that. I mean, I can read what the

14 comment says and then your lawyer can tell you

15 if I got it wrong, is about the only other

16 solution I have to that.

17 MR. SANGIAMO: That's fine.

18 BY MR. MACORETTA:

19 Q. I can read it. So can you read

20 the sentence that's talking about -- that

21 starts with "The mumps wild-type ELISA...?"

22 A. Yes, yes, yes. I can read part

23 of it, but I'm not sure I read the whole

24 thing right.

25 Q. Why don't I do the whole thing

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 2 and then your lawyer will tell me if I got it
 3 wrong.
 4 It says, "Comment (FS12): Did
 5 we really do a correlation study and if so,
 6 where is it. I don't think I have ever seen
 7 the data. If not, remove specific statement
 8 and only cite literature."
 9 So you're asking about whether a
 10 correlation study was done between the
 11 wild-type ELISA assay and the PRN assay.
 12 Right?
 13 A. I didn't remember that, yes.
 14 Q. And the answer was you didn't do
 15 a study. Correct?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: I'm not sure
 19 anymore whether I -- I mean there was
 20 this concordance analysis and a number
 21 of other analyses, so there was some
 22 sort of correlation established. They
 23 could have simply shown it to me at
 24 the time. So I -- that might have
 25 satisfied me actually.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 BY MR. MACORETTA:
 3 Q. So let me show you -- well, let
 4 me show you the next draft where this is -- I
 5 can show you the next draft where this came
 6 out. We'll show you what we're going to mark
 7 as Exhibit 20.
 8 - - -
 9 (Exhibit Schodel-20, 10/28/11 E-mail
 10 with attachment, Bates MRK-KRA00046402
 11 - 00046441, was marked for identification.)
 12 - - -
 13 BY MR. MACORETTA:
 14 Q. If you go to Page Number 28 of
 15 the draft which ends in Bates number page 430,
 16 if you look one, two, three, four, five, six,
 17 seven lines from the bottom, you'll see at the
 18 end of the line is the last two words of the
 19 previous sentence "dose and controls," and
 20 then you'll see that the sentence you have was
 21 shown to correlate the PRN assay was changed
 22 in this draft. Do you see that?
 23 A. Yes.
 24 Q. The Footnotes 29 and 30, if we
 25 look to them, cite some other literature.

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 2 They do not cite any correlation study by
 3 Merck. Right?
 4 A. Yes.
 5 Q. So does that indicate to you
 6 that there was no correlation study by Merck?
 7 MR. SANGIAMO: Object to the
 8 form.
 9 THE WITNESS: No, not
 10 necessarily. That's one of the
 11 interpretations. The other
 12 interpretation was that it hadn't been
 13 published or wasn't included and,
 14 therefore, they preferred to follow my
 15 advice if they can't produce cite
 16 literature. You just wanted to have a
 17 reference for what was done. That was
 18 all I was asking for.
 19 BY MR. MACORETTA:
 20 Q. Whatever reference they used was
 21 not some study that was done by Merck?
 22 A. That's irrelevant. I just
 23 wanted to have a reference as to whether they
 24 correlate or not.
 25 Q. The correlations we're using,

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 2 numbers 29 and 30, are papers done in 1984 and
 3 1992. Right?
 4 A. Well, this is when this was a
 5 hot topic. It's only become one with you
 6 again.
 7 Q. I'm going to go back to the --
 8 we'll use the later draft, Exhibit 20. At the
 9 bottom of -- the last line on the page we were
 10 looking at, there's a sentence that --
 11 MR. SANGIAMO: I'm sorry, John,
 12 what page is that?
 13 BY MR. MACORETTA:
 14 Q. Page ending in 430, could you
 15 read for us the sentence that starts with the
 16 word "Although" on the last line there?
 17 A. Sure. "Although being
 18 considered the 'gold standard' assay for the
 19 measurement of mumps-specific neutralizing
 20 antibodies....," gold standard in brackets,
 21 "...PRN assay is technically cumbersome and
 22 requires a large volume of serum which
 23 hampers its use in a large clinical study."
 24 Q. Do you agree with that
 25 statement?

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2 A. Yes, that's at least one of the

3 limitations.

4 Q. Well, did you agree that the PRN

5 was considered the gold standard assay for

6 measurement of mumps specific neutralizing

7 antibodies?

8 A. By some it is. And that's why

9 this is in reference marks. I mean, it's not

10 a -- that's not -- I wouldn't agree with

11 that, but it is considered that by some

12 people.

13 Q. I'm going to change topics now.

14 I'm going to show you what has previously been

15 marked as Fisher Exhibit 3. We're going to

16 talk about the house standard for a little

17 bit. Now we're marking it as 21, Schodel-21.

18 - - -

19 (Exhibit Schodel-21, E-mail

20 chain, Bates MRK-KRA01481843 -

21 01481846 & 00566614 - 00566623, was

22 marked for identification.)

23 - - -

24 BY MR. MACORETTA:

25 Q. So you can look at all of this

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2 if you want, Dr. Schodel. The only e-mail

3 from you is on the first page. I want to talk

4 to you about that, but I am going to ask you

5 about a couple other things in here. Let me

6 know when you're ready to talk about it.

7 A. Okay.

8 Q. So let me start at the back. It

9 talks about on the last page before the

10 attendees, it says, "This is a BSEC assignment

11 from the June 3 BPC meeting." So I'm going to

12 ask you what those acronyms are, BPC and BSEC?

13 A. So BPC is the Biological

14 Process Council. BSEC, I don't remember

15 exactly anymore what that stood for.

16 Q. I believe somebody said it was

17 the Biologic Standards Evaluation Committee or

18 something like that?

19 A. Sounds very reasonable but what

20 those acronyms are after many years, I don't

21 remember it.

22 Q. Were you on either of these

23 entities?

24 A. Yes, I was on BPC at times.

25 And I think I was called into BSEC probably

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2 on an ad hoc basis, not permanently. I don't

3 remember that anymore, to tell you the truth.

4 Q. There's a discussion of house

5 standard. What is the house standard as it

6 relates to the mumps vaccine?

7 A. Well, the house standard for

8 any vaccine is an internal lot of the vaccine

9 that has been very carefully assigned a

10 potency with more multiples of testing than

11 would normally be used for release to assure

12 relative accuracy. That is done repeatedly

13 over the course of a longer period of time

14 because assays tend to vary over time. And

15 then it is -- this particular lot is assigned

16 a potency out of this testing period. And

17 that particular potency is used to compare

18 the release titers when releasing a vaccine

19 so that you have something that links it back

20 to the manufacturing history.

21 Q. So the idea is that the lots in

22 the house standard, we know what their potency

23 is supposed to be. Right?

24 A. At a given point in time.

25 Q. And when we do an assay and we

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2 test both the new lot and the house standard

3 and we see how the -- what the assay says the

4 house standard is. Right?

5 A. Uh-huh.

6 Q. And then we make some correction

7 between what the assay says it is and what we

8 think it's supposed to be?

9 A. The second one is a -- can be a

10 use. And I don't know whether it is used

11 that way. That would be introducing a

12 factor. Or whether it's just simply a

13 control to establish an expected range in

14 which the new material should run without

15 actually calibrating.

16 Q. So what does --

17 A. So I don't know how it was used

18 in this particular case.

19 Q. Well, this -- the last page

20 talks about "To reach consensus on the M-M-R®

21 II House Standard which is required as part of

22 the move to potency calibration." So what's

23 potency calibration?

24 A. Well, that would be what I just

25 mentioned. What you initially assumed, that

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 2 would be the use of a house standard, not
 3 just to control but also to adjust the
 4 measured potency because of changes over time
 5 so that they're always linked to something
 6 which is as much as that's possible for
 7 biologics kept constant.
 8 Q. Around this time there's a
 9 discussion that the house standard for mumps
 10 is going to change, right, that it's going to
 11 go up by .1 log?
 12 A. Yeah, and I don't remember the
 13 details of that, but remember as we said
 14 initially in the explanation for the house
 15 standard, was house standards do change from
 16 time to time because the material comes to an
 17 end. And then you have to have enough left
 18 to test it repeatedly to compare it to the
 19 new material and to assign a new potency.
 20 And in that process there can be changes.
 21 Q. Does that mean that the number
 22 of virus particles in -- and I think
 23 Mr. Stannard who was here the other day said
 24 it's lot nine that is the house standard lot
 25 for mumps. I don't know if you know that.

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 2 A. No, I don't. I was not in
 3 manufacturing. This is way outside of my
 4 responsibilities.
 5 Q. So when we talk about changing
 6 the house standard potency, does that mean
 7 that the number of virus particles in each
 8 vial in the house standard lot has change or
 9 the assay to measure them has changed?
 10 A. It could be either/or. If
 11 the -- so the goal of the effort is always to
 12 keep the number in the product constant to
 13 the best of our knowledge. Now, in the
 14 standard, you have assay as in release, you
 15 have to deal with assay variability so the
 16 impression that you may have more or less
 17 material in there than really there is and
 18 you have to deal with the change in house
 19 standard which means moving from one
 20 manufactured lot that becomes the new house
 21 standard, from the old to the new house
 22 standard. And that may have a different
 23 assigned potency. In most cases it will
 24 because it's a different lot. So you have to
 25 do some careful analysis and to the best of

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 your knowledge and bright procedure assign a
 3 new house standard potency.
 4 Q. But over time the number of
 5 actual virus particles in those vials is not
 6 going to go up. Right?
 7 MR. SANGIAMO: Objection to --
 8 BY MR. MACORETTA:
 9 Q. In the house standard lot?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: No, but the
 13 appearance of testing can suggest that
 14 it's going up which is a strange
 15 phenomenon because of assay
 16 variability. So just like over time
 17 the vaccine doesn't really change
 18 because you make it the same way, you
 19 dilute it the same way. But you
 20 measure it repeatedly. And when you
 21 measure something repeatedly, you're
 22 also prone to the variability of any
 23 assay over time.
 24 BY MR. MACORETTA:
 25 Q. Fair enough. On the first page

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 2 of this is an e-mail from you to Roberta McKee
 3 and a bunch of other people. Right?
 4 A. Uh-huh.
 5 Q. And then it looks like somebody
 6 named Carl Burke sends your e-mail to Joye
 7 Bramble who then sends it to Keiko Simon. Do
 8 you see that right above it?
 9 A. Yeah, that looks like it.
 10 Q. So who are these -- who is Carl
 11 Burke?
 12 A. Carl Burke is an engineer who
 13 was -- where was Carl at the time? I don't
 14 know whether he was manufacturing or in
 15 analytics, but he -- probably analytics, but
 16 he was an engineer. And I think they're
 17 all -- what these three people have in common
 18 is that they're -- that they were probably in
 19 some way associated with MMR, the MMR project
 20 team that would take care of MMR issues,
 21 whereas I was primarily taking care at that
 22 time of ProQuad issues. But because they
 23 both contain MMR, these things had to be
 24 aligned and so that's how this somewhat
 25 convoluted e-mail traffic is understandable.

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2 Because one thing is done in MMR to be

3 translated into ProQuad and vice versa.

4 Q. Because at least for mumps it

5 was the same product in both?

6 A. Yes, for measles, mumps and

7 rubella it is the same product in both.

8 Q. So who is Joye Bramble? What

9 was her job at this time?

10 A. Joye Bramble is also an

11 engineer. She was for -- she was reporting

12 to me for quite a while. She was actually

13 the person responsible for developing the CTT

14 SOP for -- so basically the manufacturing

15 piece of filings. She was in my department

16 at the time. And then she was also at some

17 point in time in project management. By that

18 point in time it may be -- it's possible that

19 she was back in the biologics pilot plant.

20 She was an engineer who oversaw the biologics

21 pilot plant for quite a while. And she did

22 that after she -- after my department was

23 reassigned and some structural changes. So I

24 don't remember at that point in time where

25 she was at, was she still working with me or

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 was she already in the pilot plant.

3 Q. So were you an MM -- you were in

4 MRL. Right?

5 A. I was in MRL.

6 Q. Was Joye Bramble an MRL or an

7 MMD person?

8 A. Joye Bramble was always an MRL

9 person.

10 Q. When you said she's the project

11 manager for a point in time --

12 A. At some point in time she also

13 worked as a head of a group in project

14 management. She was also a project manager.

15 Q. Okay. So what is --

16 A. But not at this time, not

17 likely.

18 Q. So what I'm trying to understand

19 is at this time was there some person who was

20 responsible or in charge of MMR overall?

21 A. Well, you know, Merck is a

22 highly collaborative company. I don't think

23 that there is a single person that is

24 responsible for any one single product.

25 There are three different divisions that

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2 collaborate in making product. And within

3 that division a person would be responsible.

4 And she may still have been the project team

5 leader for MMR at the time. She was at that

6 at some point in time. Maybe that's where

7 this originates, but I don't remember that.

8 I don't remember the time frames. I'm very

9 bad with the exact time frames. It's a long

10 time.

11 Q. That's fine. I'm trying to

12 understand the overall structure. You said at

13 this time you were involved with ProQuad?

14 A. Yes.

15 Q. What was your -- were you in

16 charge of ProQuad or --

17 A. Well, in charge, I was -- I had

18 different functions with ProQuad. I was --

19 for quite a while I was the project team

20 co-leader of the Varicella-containing

21 vaccines which encompassed, of course,

22 ProQuad but also Zostavax and Varivax. We

23 often invited MMR folks because we had this

24 overlap of the common vaccine in ProQuad.

25 Then I was responsible for the clinical team

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2 that actually did the clinical development of

3 ProQuad. It was Barb Kuter primarily who was

4 reporting to me. And that was the extent of

5 my involvement.

6 Q. So let me try it this way: At

7 this time, June 2003 ProQuad wasn't on the

8 market yet. Right?

9 A. No.

10 Q. It hadn't been approved?

11 A. No, it hadn't even been filed,

12 I think.

13 Q. So who at Merck was in charge of

14 overseeing the various aspects of getting the

15 product, ProQuad approved?

16 A. Well, that would have been

17 essentially the regulatory liaison.

18 Q. Well, when we -- was the

19 regulatory liaison's job to say to the

20 clinical people, I need these results from

21 you, or to say -- or to make sure the

22 regulatory filings were responded to on time

23 or to do whatever else was necessary to get it

24 approved?

25 MR. SANGIAMO: Object to form.

<p style="text-align: right;">Page 390</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 THE WITNESS: In principle. I</p> <p>3 mean, that's one way of describing.</p> <p>4 Of course the whole project team knew</p> <p>5 what the expectations were, and so</p> <p>6 different jobs had to be done and</p> <p>7 different pieces were coming in and</p> <p>8 the regulatory person was ultimately</p> <p>9 responsible for collating and</p> <p>10 interacting with the agency, with the</p> <p>11 agencies, but wasn't solely</p> <p>12 responsible for the content. There</p> <p>13 were also two regulatory people, one</p> <p>14 who was on the clinical side and</p> <p>15 another one who was on the CMC side.</p> <p>16 BY MR. MACORETTA:</p> <p>17 Q. That's the manufacturing side?</p> <p>18 A. The manufacturing side.</p> <p>19 Q. So if -- let me try it this way:</p> <p>20 If the president of Merck in June 2003 wanted</p> <p>21 to know what the status of ProQuad was and</p> <p>22 where it was in getting approval, or be</p> <p>23 getting on the market, who would be the person</p> <p>24 that would have overall responsibility or</p> <p>25 would ask or would have overall responsibility</p>	<p style="text-align: right;">Page 392</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 not my responsibility.</p> <p>3 BY MR. MACORETTA:</p> <p>4 Q. So when we say the project team,</p> <p>5 the projects team, the project was to get</p> <p>6 ProQuad on the market for the ProQuad project</p> <p>7 team?</p> <p>8 A. The project for the ProQuad</p> <p>9 team was the development team, was to develop</p> <p>10 the product, get all the relevant clinical</p> <p>11 studies run, get all the relevant testing</p> <p>12 run, develop a manufacturing process and</p> <p>13 ultimately compile all the data and the</p> <p>14 information into a filing. Bring it on the</p> <p>15 market was not the -- it was not the</p> <p>16 responsibility of the project development</p> <p>17 team. That was the develop -- that is the</p> <p>18 responsibility of MMD just like manufacturing</p> <p>19 is the responsibility of the -- sorry, I have</p> <p>20 to shut down --</p> <p>21 Q. Sure. But the project team</p> <p>22 would need help from manufacturing to get the</p> <p>23 product approved. Right?</p> <p>24 A. Oh, yes, of course.</p> <p>25 Q. So earlier there was a lot of</p>
<p style="text-align: right;">Page 391</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 for that?</p> <p>3 MR. SANGIAMO: Object to the</p> <p>4 form. Calls for speculation.</p> <p>5 THE WITNESS: I don't really</p> <p>6 know. I mean, as a project team</p> <p>7 co-leader, I would probably be</p> <p>8 involved in that. I mean, it depends</p> <p>9 on where the issues are.</p> <p>10 BY MR. MACORETTA:</p> <p>11 Q. So who coordinated the issues</p> <p>12 between manufacturing and regulatory -- and</p> <p>13 MRL regulatory?</p> <p>14 A. Well --</p> <p>15 MR. SANGIAMO: I'm sorry, John,</p> <p>16 are you saying between manufacturing</p> <p>17 regulatory and MRL regulatory?</p> <p>18 MR. MACORETTA: I'll start with</p> <p>19 that, yeah.</p> <p>20 MR. SANGIAMO: Go ahead.</p> <p>21 THE WITNESS: That, I don't</p> <p>22 really know. I mean, they came up in</p> <p>23 the project team and ultimately each</p> <p>24 function was responsible to get their</p> <p>25 issues sorted out. So regulatory was</p>	<p style="text-align: right;">Page 393</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 discussion about some of the exhibits we</p> <p>3 looked at. Should we say -- what do we say in</p> <p>4 response to the FDA when they ask the question</p> <p>5 should we include this information or not</p> <p>6 include that information? Who makes the</p> <p>7 ultimate decision about we're saying this,</p> <p>8 we're not saying this? Is that the person</p> <p>9 signing the letter?</p> <p>10 MR. SANGIAMO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: This is not a</p> <p>13 question I can really answer. It</p> <p>14 depends on what the content is. I</p> <p>15 mean, obviously the person who signs</p> <p>16 the letter is responsible for what's</p> <p>17 written in the letter, but every</p> <p>18 department within Merck would be</p> <p>19 responsible for the veracity of its</p> <p>20 contribution to these filings. So,</p> <p>21 you know, in the CMC section you will</p> <p>22 have statements that come from</p> <p>23 manufacturing, in the clinical section</p> <p>24 you would have statements that come</p> <p>25 from clinical. And ultimately</p>

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 2 clinical would be responsible for the
 3 veracity of those statements. Then
 4 there is a layer of quality assurance
 5 and quality control where source
 6 documents are checked against the
 7 final document and the people who do
 8 that are responsible that everything
 9 is actually truthfully transcribed and
 10 transmitted. So they're responsible
 11 for that particular piece. If I give
 12 them wrong data, they're responsible
 13 for having them wrong in the filing,
 14 but I'm responsible if the data are
 15 wrong.
 16 BY MR. MACORETTA:
 17 Q. So the way you're describing it,
 18 then, there isn't one person who has overall
 19 responsibility?
 20 A. Below the president of Merck or
 21 MRL for that matter, not really, no. I mean,
 22 the regulatory person takes a higher degree
 23 of responsibility than anybody else in that
 24 chain because they're the direct counterparts
 25 to the agencies. But ultimately if it's a

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 2 matter of data, they would have to concur,
 3 there would have to be concurrence.
 4 Q. That's right. Okay. All right.
 5 Now I want to talk about your e-mail here that
 6 we looked at. You're talking about the
 7 points, I think, on Roberta McKee's e-mail
 8 right below yours which goes on to the
 9 following page. The end of the first
 10 paragraph, you have a sentence that says, "The
 11 responses should also be revised to explain
 12 the changed interpretation of the compendial
 13 spec that follows from house standard
 14 reassignment and why we think it is o.k. to do
 15 that." What does that mean?
 16 A. It sounds very good, but I
 17 don't really remember exactly what that
 18 means.
 19 Q. Well, okay.
 20 A. I mean a compendial spec would
 21 be something that is written into a
 22 compendium such as, for example, the European
 23 pharmacopeia with 3.7 for mumps. I don't
 24 really remember why I thought at the time
 25 that a house standard reassignment might

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 2 change the compendial spec. I don't know.
 3 Maybe I'm talking about something else. It's
 4 out of context. I don't remember the details
 5 of these discussions. Remember this was
 6 manufacturing, I was just one voice sometimes
 7 as an outsider and sometimes as somebody who
 8 did not completely understand what they were
 9 talking about.
 10 Q. So I guess I should ask then why
 11 do you get to have an opinion on this, why
 12 were you giving this opinion?
 13 A. Well, because I was in between
 14 the different projects and there were not so
 15 many people that were. And also because I
 16 had a background in the assays. But, you
 17 know, there are pieces to that which I just
 18 simply don't know.
 19 Q. So who would -- who is the
 20 expert on the house standard assignment?
 21 A. At the time it would have been
 22 Roberta. I mean, Roberta was the regulatory
 23 person in MMD.
 24 Q. And her equivalent at this time
 25 would have been Alison Fisher for MRL. Right?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. No. No. Her equivalent would
 3 have been Keith Chirgwin probably.
 4 Q. In the next sentence you talk
 5 about retaining the measles overfill. And
 6 then you say at the end of that line, "...you
 7 could as well use the 0.1 you gain on mumps
 8 now to claim a 24 months shelf-life."
 9 Do you see that?
 10 A. Yes.
 11 Q. What does that refer to?
 12 A. I don't even remember whether
 13 this refers to ProQuad or whether it refers
 14 to MMR. So I truthfully cannot tell you.
 15 But if -- so I have to speculate. I mean, if
 16 you have a .1 gain --
 17 MR. SANGIAMO: Wait.
 18 BY MR. MACORETTA:
 19 Q. Go ahead, you can answer.
 20 MR. SANGIAMO: I'm going to
 21 object. Jeff told him he's not
 22 supposed to speculate.
 23 BY MR. MACORETTA:
 24 Q. You can speculate. Go ahead.
 25 MR. SANGIAMO: No, no. If this

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 is speculation --
 3 MR. MACORETTA: Come on, you
 4 can't stop the guy in the middle of
 5 his answer because you don't like it.
 6 MR. SANGIAMO: I don't know what
 7 his answer is.
 8 MR. MACORETTA: Well, we're
 9 going to find out.
 10 MR. SANGIAMO: Well, no. He
 11 just said he's going to be
 12 speculating. Jeff, your colleague,
 13 told him at the beginning don't
 14 speculate.
 15 MR. MACORETTA: Unless he asked
 16 him to.
 17 BY MR. MACORETTA:
 18 Q. If you feel you can speculate to
 19 answer that question, please go ahead,
 20 Dr. Schodel.
 21 MR. SANGIAMO: Do not speculate
 22 in your testimony, Dr. Schodel.
 23 THE WITNESS: Okay.
 24 BY MR. MACORETTA:
 25 Q. Let me try -- we'll do it this

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 way: It says, "...to claim a 24 months
 3 shelf-life." Wasn't it always the case that
 4 every mumps vaccine Merck sold in the United
 5 States had a 24-month shelf life?
 6 A. As I just said, I don't
 7 remember whether this applied to MMR or
 8 ProQuad. ProQuad hadn't been filed anywhere
 9 so it didn't have any shelf life.
 10 Q. Let's look at the back. Do you
 11 know, what the -- the next page, the third
 12 bullet point in Ms. McKee's e-mail. "Quickly
 13 prepare and submit the mumps supplement to
 14 reduce expiry to 18 months...." Do you know
 15 what she's talking about there?
 16 A. No, I don't remember that
 17 anymore.
 18 Q. Well, is it -- you're in charge
 19 of ProQuad. Was there a discussion that there
 20 was going to be an 18 months as opposed to a
 21 24-month shelf life?
 22 MR. SANGIAMO: Object to the
 23 form.
 24 THE WITNESS: I don't remember
 25 that.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 BY MR. MACORETTA:
 3 Q. Do you ever remember any
 4 discussion about having a shelf life less than
 5 24 months for MMR?
 6 A. With the exception of what we
 7 had discussed before, no.
 8 Q. What was it we had discussed
 9 before?
 10 A. The stability data e-mails that
 11 were just moved around.
 12 Q. When you say, "...the 0.1 you
 13 gain on mumps now....," does that mean that
 14 because house standard potency has gone up by
 15 .1 log?
 16 A. I don't know. I would -- it
 17 seemed to me, but, again, I'm extrapolating
 18 from my own sentences, that there is a gain
 19 in .1 through end expiry which may well mean
 20 that the .1 loss before was due to a
 21 different house standard calibration or it
 22 was due to an error in house standard
 23 calibration. So by doing it more properly,
 24 you actually gained one log. So you had less
 25 loss.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. So the house standard was
 3 recalibrated in a way that added .1 log?
 4 A. I don't know that. It could
 5 have, as far as the house standard was
 6 concerned, gone down but the net result would
 7 be that you -- in the modeling you gain .1 in
 8 potency.
 9 Q. If the house standard goes down,
 10 how does the potency go up?
 11 A. Because you calibrate it to the
 12 house standard.
 13 Q. But if it's calibrated before
 14 and after you change the house standard and
 15 the house standard goes down, how could the
 16 potency go up?
 17 A. Well, because it's relative to
 18 the house standard. So if your assay
 19 point -- it goes in the other direction
 20 essentially. I mean, you calibrate it to the
 21 house standard. So if your -- if you do a
 22 calibration, you use the same measure over
 23 and over again and you calibrate it in the
 24 direction that the standard is going.
 25 Q. So if the standard yesterday was

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 3.7 and it's 3.6 today, that means that a lot
 3 that we thought was 3.7 yesterday, we now
 4 think is 3.6. Right?
 5 A. Not necessarily. You measure
 6 the same amount twice. Now it appears to be
 7 lower. So you put in more to get to the same
 8 number.
 9 Q. You put in more product to get
 10 to the same number?
 11 A. Well, your release number goes
 12 up. The same number appears to be higher.
 13 It's a bit counterintuitive, but it --
 14 Q. It is. And that's what if the
 15 release spec for this -- let's assume --
 16 A. That's at least -- I mean, I'm
 17 not the specialist on house standard for MMD.
 18 I was never in manufacturing. So that's a
 19 speculation that I would make. But I don't
 20 know how it was exactly used in calibration,
 21 so...
 22 Q. I'm just asking you how you used
 23 it here?
 24 A. Well, I just use -- I didn't --
 25 that didn't -- it didn't -- for me, in this

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 particular statement, it was simply stating
 3 that if you have a better measure now,
 4 whatever that is, not opining on the house
 5 standard, that let's you show with credible
 6 data that you have .1 log more than you
 7 thought before in the product through end
 8 expiry, then that also means that actually
 9 the product will have a longer shelf life.
 10 Q. Then the next paragraph you say,
 11 "I'm still not sure how the ProQuad filing
 12 will be handled as you go forward and change
 13 the mumps specs without changing the mumps
 14 maximum release spec in the ProQuad file which
 15 is supposed to reference the MMR license...."
 16 Do you see that?
 17 A. Uh-huh.
 18 Q. The idea is that ProQuad is
 19 going to reference the MMR license for the
 20 specifications of the M, M and R parts of
 21 ProQuad. Right?
 22 A. Yes.
 23 Q. So it's going to be the same
 24 release spec for mumps in MMR as it is for
 25 ProQuad. Right?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Correct.
 3 Q. The same end expiry potency.
 4 Right?
 5 A. Correct.
 6 Q. Because it's the same product,
 7 right, the mumps bulk is made -- it's the same
 8 mumps bulk for MMR as it is for ProQuad.
 9 Right?
 10 A. Correct.
 11 Q. Okay. So now you're asking here
 12 if you change -- when you say change the mumps
 13 specs, you're talking about changing something
 14 because the house standard changes. Right?
 15 A. I'm not sure. This could be
 16 referring to house standard or it could be
 17 referring to the changes that we discussed
 18 previously with the introduction of a
 19 different view of CBER on what an end expiry
 20 means and, therefore, as a result and
 21 relative overfill that was done since '99
 22 from what I saw in these documents. And I
 23 think that some of these changes in data for
 24 MMR had not made their way into the ProQuad
 25 manufacturing documentation yet. And,

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 therefore, I was just asking the question if
 3 we have agreement that they're the same, how
 4 are we going to introduce the changes that
 5 which you're currently working on at MMR for
 6 the agency, how are we going to introduce
 7 them into ProQuad to make sure that they
 8 remain the same.
 9 Q. What's the ultimate answer to
 10 that question?
 11 A. I don't know.
 12 Q. Well, you were -- when did you
 13 stop working on ProQuad?
 14 A. When did I stop working on
 15 ProQuad? I mean, I think I probably
 16 completely stopped working on ProQuad 2008 or
 17 2009 or so. This was not the same level of
 18 attention anymore.
 19 Q. Let me show you what we're going
 20 to mark as Schodel-22.
 21 MR. MACORETTA: How much time do
 22 we have left?
 23 VIDEOGRAPHER: About 21 minutes.
 24 MR. MACORETTA: Thank you.
 25 - - -

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 (Exhibit Schodel-22, 2/25/03
 3 E-mail, Bates MRK-KRA00566606, was
 4 marked for identification.)
 5 - - -
 6 BY MR. MACORETTA:
 7 Q. All right. Let me know when
 8 you've had a chance to look at this.
 9 A. Yeah, I've looked at that. Not
 10 completely yet.
 11 Q. The top e-mail is from you to
 12 Tim Schofield. Do you see that?
 13 A. Uh-huh.
 14 Q. And it says, "so...you can see
 15 the presentation in addition to my diatribe."
 16 What diatribe are you talking about?
 17 A. I have no idea. Tim and I
 18 talked about stuff. I may have told him
 19 something about anything.
 20 Q. Okay. And this says -- the
 21 e-mail below says the subject matter is "MMR
 22 House Standard assignment discussion," and it
 23 says, "Attached please find slides that were
 24 to be shown for tomorrow's Net Meeting...."
 25 Do you see that?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Uh-huh.
 3 Q. What's a net meeting?
 4 A. Probably a meeting over the
 5 Internet.
 6 Q. Okay.
 7 A. Or the intranet.
 8 Q. Okay. Were you involved at all
 9 in creating any of these slides?
 10 A. Nope. This is manufacturing
 11 stuff. This is not my direct responsibility
 12 at all.
 13 Q. I got it. I understand that,
 14 but you looked at it and passed it on and had
 15 a diatribe about it apparently.
 16 A. Or I had a diatribe unrelated
 17 to that.
 18 Q. Maybe.
 19 A. Much more likely actually.
 20 Q. So -- well, let me start at the
 21 first page of the slide, the first one. It
 22 says -- there's a question from CBER, please
 23 give data concerning house standard potency
 24 values obtained. Then it says, "In
 25 preparation to answer question, recognized MuV

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 HS assigned value differs from historic
 3 performance."
 4 Do you see that?
 5 A. Yeah, I see that.
 6 Q. What is MuV?
 7 A. Mumps virus.
 8 Q. What does it mean that its
 9 assigned value differs from historic
 10 performance?
 11 A. That it's being given a value
 12 in -- when as we discussed before, in that
 13 crossover period when it was assigned a
 14 value, that is different from historic
 15 performance of that same house standard.
 16 Q. So when you say assigned value,
 17 is that house standard?
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: Yeah.
 21 BY MR. MACORETTA:
 22 Q. So recognized mumps, MuV HS
 23 assigned value, that's the house standard
 24 value?
 25 A. That's the house --

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 MR. SANGIAMO: Object to the
 3 form.
 4 THE WITNESS: That's the house
 5 standard value that was assigned at a
 6 given period in time when that house
 7 standard was introduced.
 8 BY MR. MACORETTA:
 9 Q. Then it says, "...differs from
 10 historic performance." What does that mean,
 11 when you measure the potency of a lot -- what
 12 does that mean?
 13 MR. SANGIAMO: Object to the
 14 form.
 15 THE WITNESS: Well, it means --
 16 look onto 616 and you can see what
 17 that means. So you'll see here
 18 historic performance of house
 19 standards, and you see that it
 20 measures as 4.2, 4.3, 4.1, up to 4. --
 21 4.4, down to 4.2. This is different
 22 data points from '95 to '02. And then
 23 it was assigned a value. And the
 24 problem is that it apparently
 25 fluctuated or differed from that

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 assigned value which is not too
 3 surprising in these things because
 4 assays do change, and they change
 5 unfortunately in sometimes long
 6 periodicities. You will sometimes
 7 have an assay that for unknown reasons
 8 runs a little different in the summer
 9 period or in a given year than in
 10 another year. Now, if you have a
 11 long-time assigned potency for a house
 12 standard, that has long-time
 13 consequences on manufacturing.
 14 BY MR. MACORETTA:
 15 Q. And it looks like -- I'm going
 16 to go back to page 615, the previous page
 17 under "How are potencies assigned," it seems
 18 to say for mumps that the house standard
 19 assigned was 4.2. Right?
 20 A. Yeah, that's what it says here.
 21 Q. But there's a -- when it says
 22 limits plus or minus .3, that's the
 23 variability. Right?
 24 A. Those are controlled limits,
 25 not necessarily variability.

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 Q. Well, if we look back on 416,
 3 this would show us the variability. Right?
 4 We see some tasks as high as 4.8 and some down
 5 to 3.8. Right?
 6 A. Now you're on 16?
 7 Q. Yes.
 8 A. On the lower half. Yeah, I
 9 mean, I see it going from 4.1 up to -- I
 10 mean, I was looking at the average line but
 11 if you look at the individual data points,
 12 yes, you can see anything from 3.9 up to 4.8
 13 or so. Or 3. -- you were right, 3.8 even.
 14 Q. So that's like a variability of
 15 .4. Right?
 16 A. From 3.8 to 4.8, that's almost
 17 a log variability.
 18 Q. That's almost a what?
 19 A. That's almost a log.
 20 Q. And a log is ten times. Right?
 21 A. Yes.
 22 Q. So when we -- so variability --
 23 so when we change the log .1, that means
 24 that's 25 percent more or less product. Right?
 25 A. You could see it that way,

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 yeah.
 3 Q. Would you consider that a lot of
 4 variability for a house standard test, a one
 5 log?
 6 A. The question is here more --
 7 MR. SANGIAMO: The object to the
 8 form.
 9 THE WITNESS: The question is
 10 here -- well, first of all, it's not
 11 really my field to opine on. I -- the
 12 question here is more does it behave
 13 differently in different periods of
 14 time.
 15 BY MR. MACORETTA:
 16 Q. Well, this is showing that it
 17 behaves, the period of time for these tests is
 18 over what, seven years, '95 to '02?
 19 A. Yeah.
 20 Q. If we look at 615, the top
 21 chart, it says, "What are the assigned
 22 potencies," and then for mumps it has
 23 "Assigned Potency* 4.2 (4.9)."
 24 Now, is that the difference
 25 between a .1 mL and a per dose?

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL
 2 A. Yes.
 3 Q. And if I'm reading Table 2 on
 4 page 615 right, they did 32 runs to come up
 5 with the house standard. Is that what that
 6 means?
 7 A. You know, that's what it could
 8 mean, but I don't know that. These are
 9 obviously not data that I have generated or
 10 am that familiar with. So, for example, I
 11 can't tell you how many multiples are in
 12 there. So anyway.
 13 Q. But if you were in charge of --
 14 since you were in charge of ProQuad at this
 15 time, you had responsibility for ProQuad, how
 16 the house standard was calculated and applied
 17 was an issue for you, wasn't it?
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: In principle, no,
 21 as long as it remained stable. If it
 22 led to a change in the product or a
 23 change in how the product was made,
 24 then potentially yes.
 25 BY MR. MACORETTA:

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. But the application and

3 calculation of the house standard was something

4 that CBER had to know about. Right?

5 A. Yes, of course.

6 Q. If you could go to the next --

7 to the -- let's go to the last page, the

8 "Summary" page. The second bullet point says,

9 "...there is general agreement...with the

10 exception of mumps."

11 Then the third bullet point says

12 house standard increases from 4.2 to 4.3 is

13 technically defensible.

14 A. This is the very last one, I

15 see.

16 Q. Yes. I'm sorry. Do you know

17 what that means, "is technically defensible"?

18 MR. SANGIAMO: Objection. Calls

19 for speculation.

20 MR. MACORETTA: I just asked him

21 if he knew what it meant.

22 MR. SANGIAMO: You're acting

23 like he wrote the document.

24 MR. MACORETTA: That's fine.

25 BY MR. MACORETTA:

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 Q. You can answer the question.

3 A. I mean, the only thing I can

4 see here and you can see that for yourself is

5 on 618, if you look at all the data, you have

6 a total number of 2,900 runs and you have an

7 average of 4.28. So that is how the house

8 standard has behaved. Then you have the

9 qualification data that were done over a

10 limited period of time with a limited number

11 of runs and that resulted in an assignment of

12 4.2. That's different. And, therefore, the

13 defense of that change would be the now

14 available very large quantity of data that

15 suggested that the house standard may have

16 been assigned too low a potency and should be

17 increased.

18 Q. So it goes from 4.2 to 4.3?

19 A. That is correct.

20 Q. But the release potency does

21 not -- the minimum and maximum release

22 potencies do not change. Right? It's still

23 5.0 or 5.5. Right?

24 A. They don't change.

25 Q. Well, but aren't you putting

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 more virus particles in the same product if

3 you don't change the release potencies but the

4 house standard recognizes there's more product

5 in it?

6 A. No. No, you just call it a

7 different number.

8 Q. So it's the same --

9 A. You do exactly the same thing.

10 Q. It's the number --

11 A. The manufacturing process

12 remains stable. It remains exactly the same

13 dilutions. Exactly what you've done before.

14 The difficulty here is really one that is

15 related to the accuracy of an assay of

16 measuring whether or not it meets release

17 specifications. You don't put in more or

18 less. You just call it a different number.

19 Q. So what was 5 yesterday is 5.1

20 today?

21 A. In view of more data what you

22 measured as 5 yesterday you now realize is in

23 reality 5.1.

24 Q. But if my release spec is 5.0,

25 isn't -- if I measured something at 4.9

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1 FLORIAN SCHODEL, MD - CONFIDENTIAL

2 yesterday, that's 5.0 today. Right?

3 A. Well, I'm not sure I follow.

4 Q. You know what, strike that. Let

5 me -- I'll withdraw that question.

6 Let's look at the last bullet

7 point. Mumps house standard assigned potency

8 has important impact on - MMR II near-term

9 manufacturability. What does that mean?

10 A. To tell you the truth, I don't

11 exactly know, but -- I don't know.

12 Q. You just said that nothing

13 changes, it's just a change in the number. If

14 nothing changes, why would it impact

15 manufacturability?

16 A. I mean, you -- I don't know. I

17 mean, you may -- I really don't know.

18 Q. This would be something that you

19 would want to know about, right, since you're

20 in charge of ProQuad?

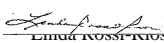
21 A. Yeah, absolutely.

22 MR. SANGIAMO: Object to the

23 form.

24 BY MR. MACORETTA:

25 Q. Okay. And it also says, "MMR®II

<p style="text-align: right;">Page 418</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 shelf-life, recon/store time," and "calibrated</p> <p>3 stability." Do you have an understanding of</p> <p>4 why changing the house standard potency would</p> <p>5 impact them?</p> <p>6 A. Yeah. That -- we just</p> <p>7 discussed that, because the numbers that you</p> <p>8 assign to the potencies at given points in</p> <p>9 time change with a calibration to the house</p> <p>10 standard. The house standard is different,</p> <p>11 they go up or down.</p> <p>12 Q. So does that mean that if my end</p> <p>13 expiry potency was 4.2 yesterday, it's 4.3</p> <p>14 today when we increase the house standard?</p> <p>15 A. No, it's still 4.3.</p> <p>16 Q. No, it's if 4.2 yesterday. 4.0.</p> <p>17 Let's say if I --</p> <p>18 A. You're not changing the end</p> <p>19 expiry potency, we're just changing what</p> <p>20 number we give the measurement.</p> <p>21 Q. So the end expiry potency is the</p> <p>22 same but what measured 4.2 yesterday measures</p> <p>23 at 4.3 today?</p> <p>24 A. It may still measure at 4.3,</p> <p>25 but it gets calibrated to a differently</p>	<p style="text-align: right;">Page 420</p> <p>1 CERTIFICATE</p> <p>2</p> <p>3</p> <p>4</p> <p>5 I do hereby certify that I am a Notary</p> <p>6 Public in good standing, that the aforesaid</p> <p>7 testimony was taken before me, pursuant to</p> <p>8 notice, at the time and place indicated; that</p> <p>9 said deponent was by me duly sworn to tell</p> <p>10 the truth, the whole truth, and nothing but</p> <p>11 the truth; that the testimony of said</p> <p>12 deponent was correctly recorded in machine</p> <p>13 shorthand by me and thereafter transcribed</p> <p>14 under my supervision with computer-aided</p> <p>15 transcription; that the deposition is a true</p> <p>16 and correct record of the testimony given by</p> <p>17 the witness; and that I am neither of counsel</p> <p>18 nor kin to any party in said action, nor</p> <p>19 interested in the outcome thereof.</p> <p>20</p> <p>21 WITNESS my hand and official seal this</p> <p>22 5th day of January, 2017.</p> <p>23</p> <p>24</p> <p>25</p> <p style="text-align: center;">  Linda Ross-Rios, RPR, CSR Notary Public </p>
<p style="text-align: right;">Page 419</p> <p>1 FLORIAN SCHODEL, MD - CONFIDENTIAL</p> <p>2 assigned house standard and, therefore, it</p> <p>3 gets called a different number with more</p> <p>4 data.</p> <p>5 Q. Okay.</p> <p>6 A. I think we're coming to the</p> <p>7 end --</p> <p>8 MR. MACORETTA: That's fine. We</p> <p>9 are. And I'm not going to start and</p> <p>10 do something else. I don't have any</p> <p>11 more questions today, Dr. Schodel.</p> <p>12 THE WITNESS: Thank you.</p> <p>13 MR. MACORETTA: Thank you.</p> <p>14 MR. SANGIAMO: No questions</p> <p>15 here.</p> <p>16 VIDEOGRAPHER: The time now is</p> <p>17 5:57. This concludes the deposition.</p> <p>18 End of disc six of six.</p> <p>19 - - -</p> <p>20 (Witness excused.)</p> <p>21 - - -</p> <p>22 (Deposition concluded at</p> <p>23 5:57 p.m.)</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 421</p> <p>1 INSTRUCTIONS TO WITNESS</p> <p>2 Please read your deposition over</p> <p>3 carefully and make any necessary corrections.</p> <p>4 You should state the reason in the</p> <p>5 appropriate space on the errata sheet for any</p> <p>6 corrections that are made.</p> <p>7 After doing so, please sign the errata</p> <p>8 sheet and date it.</p> <p>9 You are signing same subject to the</p> <p>10 changes you have noted on the errata sheet,</p> <p>11 which will be attached to your deposition.</p> <p>12 It is imperative that you return the</p> <p>13 original errata sheet to the deposing</p> <p>14 attorney within thirty (30) days of receipt</p> <p>15 of the deposition transcript by you. If you</p> <p>16 fail to do so, the deposition transcript may</p> <p>17 be deemed to be accurate and may be used in</p> <p>18 court.</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>

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1 ACKNOWLEDGMENT OF DEPONENT

2

3 I have read the foregoing transcript of

4 my deposition and except for any corrections or

5 changes noted on the errata sheet, I hereby

6 subscribe to the transcript as an accurate record

7 of the statements made by me.

8

9 _____

10 FLORIAN SCHODEL, MD

11

12 SUBSCRIBED AND SWORN before and to me

13 this ____ day of _____, 20__.

14

15

16 _____

17 NOTARY PUBLIC

18

19

20 My Commission expires:

21

22

23

24

25

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1 ERRATA SHEET

2 IN RE: USA ex rel. vs. MERCK

3 DATE: 12/22/2016

4 PAGE	LINE	CORRECTION AND REASON
5	_____	_____
6	_____	_____
7	_____	_____
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22	_____	_____
23	_____	_____
24	_____	_____
25	(DATE)	FLORIAN SCHODEL, MD

10/25/2019
Declaration of G. Reilly
EXHIBIT 117

To: 'Y. Kino'[kino-yo@kaketsuken.or.jp]; Morsy, Manal A.[manal_morsy@merck.com]
Cc: Chirgwin, Keith D.[keith_chirgwin@merck.com]; Bramble, Joye L.[joye_bramble@merck.com]; Matthews, Holly[holly_matthews@merck.com]; Heyse, Joseph F.[joseph_heyse@merck.com]; Schodel, Florian[florian_schodel@merck.com]; Simon, Keiko[keiko_simon@merck.com]; Musey, Luwy[luwuy_musey@merck.com]; Schofield, Timothy L[timothy_schofield@merck.com]; Antonello, Joseph M[joseph_antonello@merck.com]; Galinski, Mark S.[mark_galinski@merck.com]; Abraham, Katalin G.[katalin_abraham@merck.com]; Shaw, Alan[alan_r_shaw@merck.com]; 'Shiosaki'[shiosaki@kaketsuken.or.jp]; 'Funatsu'[funatsu-ma@kaketsuken.or.jp]; 'Kanehara'[kanehara@kaketsuken.or.jp]; 'Timothy A. Corrigan'[corrigan@kaketsuken.or.jp]; 'Tochihara'[tochihara@kaketsuken.or.jp]; '????'[sakai-kaz@kaketsuken.or.jp]; '????'[mizuno@kaketsuken.or.jp]; '????'[tanaka@kaketsuken.or.jp]; '?? ??'[honda@kaketsuken.or.jp]; '?? ??'[mizokami@kaketsuken.or.jp]
From: Morsy, Manal A.
Sent: Fri 9/13/2002 9:59:17 AM
Importance: Normal
Subject: RE: Kaketsuken Questions regarding mumps end expiry potency

No trouble at all – in terms of the rHA history – I will have to get back to you on this one – for correction rHA is not a virus stabilizer – but rather like FBS, rHA is required for maintaining the mono-layer cell culture integrity.

in terms of the clinical trial – the study was designed to address a specific request made to us by the EU since rHA is a recombinant excipient to show that anti –HA antibodies are not generated.

in terms of why PRN and ELISA in the mumps end expiry and only ELISA in the MMRII/rHA – and this CBER's explanation because we asked the same question regarding the need for a PRN – CBER considers a neutralization assay essential for establishing efficacy were you need to define effectiveness for a product – the mumps end expiry trial is comparing release to expiry within the same product – however when you are comparing equivalence between two products – CBER considers ELISA sufficient.

Manal

-----Original Message-----

From: Y. Kino [mailto:kino-yo@kaketsuken.or.jp]
Sent: Friday, September 13, 2002 4:21 AM
To: 'Morsy, Manal A.'
Cc: 'Chirgwin, Keith D.'; 'Bramble, Joye L.'; 'Matthews, Holly'; 'Heyse, Joseph F.'; 'Schodel, Florian'; 'Simon, Keiko'; 'Musey, Luwy'; 'Schofield, Timothy L'; 'Antonello, Joseph M'; 'Galinski, Mark S.'; 'Abraham, Katalin G.'; 'Shaw, Alan'; 'Shiosaki'; 'Funatsu'; 'Kanehara'; 'Timothy A. Corrigan'; 'Tochihara'; '????'; '????'; '????'; '?? ??'; '?? ??'
Subject: RE: Kaketsuken Questions regarding mumps end expiry potency

Manal,

Thank you very much for your clarifications.

I understand that rHA is in a completely different category from FCS, because rHA is contained in the virus growth media and the stabilizer for the virus harvests, but FCS is not. However, I also understand that it is not appropriate to describe the M–M–R(TM)II with rHA as a "new formulation".

Because rHA is not a final excipient, a clinical study and even a partial change application would not be required upon replacement, as you previously expected. However, as a matter of fact, you are conducting a clinical study and are going to make a partial change application; therefore, the change of HSA from plasma-derived to recombinant is not supposed to be a mere replacement of one of the materials.

Because we also have to make a partial change application regarding rHA in Japan, I would appreciate it if you could summarize the history

of rHA replacement, especially the reason for the clinical trial and partial application. I am not in a hurry for this.

Finally, I do not understand the end of the last paragraph of your e-mail of September 12th. "...in both the primary and secondary endpoint..." I understand the protocol of the mumps dose justification study in that there are two endpoints, PRN and ELISA; however, in the clinical study with MMRII/rHA, you employ only ELISA. In that sense, the two studies are not the same. My question is, why only ELISA was accepted for MMRII/rHA whereas both PRN and ELISA were required for the mumps end expiry trial. I really need your explanation on this point. I am very sorry to trouble you, but I would like to clarify the situation before holding our internal meeting.

I would appreciate your response.

Regards,

Yoichiro

-----Original Message-----

From: Morsy, Manal A. [mailto:manal_morsy@merck.com]

Sent: Thursday, September 12, 2002 11:16 PM

To: 'Y. Kino'; Morsy, Manal A.

Cc: Chirgwin, Keith D.; Bramble, Joye L.; Matthews, Holly; Heyse, Joseph F.; Schodel, Florian; Simon, Keiko; Musey, Luwy; Schofield, Timothy L; Antonello, Joseph M; Galinski, Mark S.; Abraham, Katalin G.; Shaw, Alan; Shiosaki; Funatsu; Kanehara; Timothy A. Corrigan; Tochiara; ???; ???; ???; ?? ??; ?? ??

Subject: RE: Kaketsuken Questions regarding mumps end expiry potency

Dear Yoichiro,

In terms of the 20,000 CCID50 and rationale – I will have to defer answering until we review the papers you are referring to – also please keep in mind that we are still evaluating the shelf life and what we (Merck) can support – so please think of that as one of the potential options that may or may not be viable once we complete our shelf life evaluation.

Also please note that the rHA replacement in MMRII is NOT a "new formulation" rather this is a bulk culture media excipient like fetal bovine serum which is what it is actually replacing in the bulk process when the virus infection is initiated, not a "formulation" excipient in the final container for stability. We have to make sure that there is clarity on this issue other wise this can lead to great confusion especially in agency communications.

In terms of your question – if we were going to conduct another end expiry trial for the MMRII/rHA – the answer as previously stated is NO – MMRII/rHA is the same as the current MMRII except for the excipient replacement – therefore what ever the end expiry assignment becomes for the the current MMRII is what would translate to minimum potency for MMRII/rHA – ie what ever the results are for the ongoing mumps end expiry trial are will affect current label and will be transferred to revised label for MMRII/rHA.

The criteria in the MMRII/rHA study are the same except the assays used are exclusively ELISA – ie the PRN (plaque reduction neutralization) assay is not used to evaluate immune response for mumps in the MMRII/rHA study. Recall that the primary end point in the mumps end expiry is based on measuring immune response using the PRN assay while the secondary end point in the that study is based on using the mumps ELISA assay – in both the primary and secondary end point scenarios the criteria of success are the same and are the same as those set forth for the

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MRK-KRA01386178
MRK-CHA01386178
Appx4702

MMRII/rHA.

Hope this helps.

Manal

Manal Morsy, MD, PhD, MBA
Director
Worldwide Regulatory Affairs
Vaccines/Biologics
morsy@merck.com
tel: 484-344-3785
fax: 484-344-2962

-----Original Message-----

From: Y. Kino [mailto:kino-yo@kaketsuken.or.jp]
Sent: Thursday, September 12, 2002 4:59 AM
To: 'Morsy, Manal A.'
Cc: 'Chirgwin, Keith D.'; 'Bramble, Joye L.'; 'Matthews, Holly'; 'Heyse, Joseph F.'; 'Schodel, Florian'; 'Simon, Keiko'; 'Musey, Luwy'; 'Schofield, Timothy L.'; 'Antonello, Joseph M.'; 'Galinski, Mark S.'; 'Abraham, Katalin G.'; 'Shaw, Alan'; Shiosaki; Funatsu; Kanehara; Timothy A. Corrigan; Tochiwara; ????; ????; ????; ?? ??; ?? ??
Subject: RE: Kaketsuken Questions regarding mumps end expiry potency

Dear Manal,

Thank you very much for your quick response. The following are several additional questions I have for you:

Regarding Question #3, originally, we were going to use the results of your ongoing trial as a rationale for the end expiry potency of mumps; however, if we submit the JNDA with 20,000 CCID50, we will have to use another rationale. In such a situation, we will have to use the minimum immunizing titer reported in papers (J.A.M.A, 203:9-13, 1968 and The New England Journal of Medicine, 278(5), 227-232,1968). Is this OK for you, or could you suggest an alternative rationale?

For me, your reply to Question #4 is unclear. Are you going to conduct an additional clinical trial to determine the end expiry potency of the new formulation? Your explanation would be appreciated.

Finally, are the criteria for the endpoint of the ongoing clinical trial using M-M-R(TM)II with rHA the same as those of the mumps dose justification trial?

I am looking forward to your complete response. Thank you.

Regards,

Yoichiro

-----Original Message-----

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MRK-KRA01386179
MRK-CHA01386179
Appx4703

From: Morsy, Manal A. [mailto:manal_morsy@merck.com]
Sent: Thursday, September 12, 2002 2:49 AM
To: 'Y. Kino'
Cc: Chirgwin, Keith D.; Bramble, Joye L.; Matthews, Holly; Heyse, Joseph F.; Schodel, Florian; Simon, Keiko; Musey, Luwy; Schofield, Timothy L; Antonello, Joseph M; Galinski, Mark S.; Abraham, Katalin G.; Shaw, Alan
Subject: RE: Kaketsuken Questions regarding mumps end expiry potency

Dear Yoichiro,

Please note comments to questions – I will get back to you with complete responses as soon as possible following internal discussions.

Regards

Manal
Manal Morsy, MD, PhD, MBA
Director
Worldwide Regulatory Affairs
Vaccines/Biologics
morsy@merck.com
tel: 484-344-3785
fax: 484-344-2962

-----Original Message-----

From: Y. Kino [mailto:kino-yo@kaketsuken.or.jp]
Sent: Wednesday, September 11, 2002 3:06 AM
To: Morsy Manal
Cc: Shiosaki; Kanehara; Funatsu; Tochiara; ?????; ?????; ?? ??; ?????
Subject: Questions regarding mumps end expiry potency

Dear Manal,

As of the teleconference, we have been internally discussing possible options regarding the mumps end expiry potency. To make our discussions more concrete, I would like to confirm the following points:

1. Would it be possible to forward us the interim summary data of the study in which 265 samples were excluded? We are interested in the data for the subjects that were already fixed.
[Morsy, Manal A.] we will discuss internally and determine feasibility and timing
2. If 20,000CCID50 is adopted as the end expiry potency, do you recommend 1 year as the shelf life?
[Morsy, Manal A.] we are currently evaluating the shelf life recommendation
3. Is there any other basis regarding 20,000CCID50 as the end expiry potency other than the minimum required virus titer?
[Morsy, Manal A.] please clarify – I am not sure I understand your question.
As you recall we had previously forwarded to you the historical events that led to CBER's request that Merck conducts an end expiry trial if Merck wanted to change mumps potency in the label from 20,000. please see attached:

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MRK-CHA01386180
Appx4704

4. What is the mumps end expiry potency of the investigational vaccine with rHA which is being used in the clinical trial? Further, is the mumps sero-conversion rate one of the endpoints of the trial?[Morsy, Manal A.] yes

[Morsy, Manal A.] the investigational vaccine is tested at release – end expiry potency for mumps would follow what would be in the label post the end expiry trial conclusion.

5. When you change HSA to rHA, is an additional end expiry trial with the new formulation required?

[Morsy, Manal A.] No – see comment above

6. If the primary end point is not fulfilled and you negotiate with CBER, is there any possibility of going back to 5,000 CCID50?

[Morsy, Manal A.] unlikely the preliminary data from the mumps end expiry based on the criteria set forth by CBER would not support 5,000 – what we would negotiate if one of the two criteria is not met would be the 10,000 CCID50

We will hold an internal meeting next Wednesday to determine which option to pursue; therefore, I would appreciate it if you could forward your responses to the questions noted above by next Tuesday.

[Morsy, Manal A.] Additional comments will be provided as soon as internal discussion at our end are concluded to further address your questions.

Regards

Manal

As I explained previously, the timing of the JNDA submission is an extremely political issue both internally and externally. I would appreciate your cooperation.

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=====

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**MRK-KRA01386182
MRK-CHA01386182
Appx4706**

10/25/2019
Declaration of G. Reilly
EXHIBIT 118

To: Chodakewitz, Jeffrey A[jeffrey_chodakewitz@merck.com]; Chirgwin, Keith D.[keith_chirgwin@merck.com]; Heyse, Joseph F.[joseph_heyse@merck.com]; Schodel, Florian[florian_schodel@merck.com]; Matthews, Holly[holly_matthews@merck.com]; Willison, Barbara W[barbara_willison@merck.com]; Morsy, Manal A.[manal_morsy@merck.com]; Musey, Luwy[luwymusey@merck.com]; Dietrich, Gary J[gary_dietrich@merck.com]; Hartzel, Jonathan[jonathan_hartzel@merck.com]; Karnik, Shaila[shaila_karnik@merck.com]; Kuter, Barbara J.[barbara_kuter@merck.com]
Cc: Schreader, Nancy T[nancy_schreader@merck.com]; Kriebel, Lonnie M[lonnie_kriebel@merck.com]; Daggett, Kathleen N[kathy_daggett@merck.com]; Shay, Charlotte[charlotte_shay@merck.com]
From: Simon, Keiko
Sent: Mon 10/27/2003 8:21:49 PM
Importance: Normal
Subject: VP Clinical planning meeting information
[Final_October25_VP_PlanningMeeting_MumpsEndExpiry2004.ppt](#)
[oGOS versus GOS Comparison.ppt](#)

Dear all,

Please find attached the presentation slides from Luwy and Jon for tomorrow's discussion. Apologies for the lateness of this distribution.

Outline of Clinical documentation

GOS vs. oGOS comparison

Thank you,
Keiko

*Thank you,
Keiko O. Simon, PhD
Project Management
484-344-7590 (phone)
484-344-3659 (fax)*

M-M-R™II /Mumps End-Expiry U.S. sBLA Filing
Review of Clinical Section of CTD outline

VP Clinical Planning Meeting

October 28, 2003

Presentation Outline

- Module 2: Common Technical Document Summaries
 - 2.5: Clinical Overview
 - 2.7: Clinical Summary

- Module 5: Clinical Study Reports
 - 5.3: Clinical Study Reports
 - 5.4: Literature References

2

Presentation Outline

- Module 2: Common Technical Document Summaries
 - 2.5: Clinical Overview
 - 2.7: Clinical Summary

- Module 5: Clinical Study Reports
 - 5.3: Clinical Study Reports
 - 5.4: Literature References

3

2.5: Clinical Overview

- 2.5.1: Product Development Rationale
- 2.5.2: Overview of Biopharmaceutics
- 2.5.3: Overview of Clinical Pharmacology
- 2.5.4: Overview of Efficacy
- 2.5.5: Overview of Safety
- 2.5.6: Benefits and Risks Conclusions
- 2.5.7: List of References

4

2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
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- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

6

2.5.1.1: Pharmacological Class

- A brief description of manufacturer and indicate that vaccine is used worldwide for the prevention of measles, mumps, and rubella

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2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1.2: Chemical and Pharmaceutical Properties

- Vaccine composition as regards to how the different components are derived and reference the monovalent vaccines.
- Information will include manufacturing process, cell substrate, final product composition, and potency specifications.
- State that vaccine is sterile and used for subcutaneous injection.

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2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1.3: Current and Targeted Indications

- State that present submission will not propose any change to the vaccine's indication, but rather sought to reduce the expiry potency for mumps component of M-M-R™II from 4.3 to 4.1 log₁₀TCID₅₀/dose
- Provide the current indication against the 3 diseases
- Recommended schedule in the United States and precautions for some subjects with history of anaphylactic reaction to any vaccine component
- State that marketed application never been rejected nor withdrawn for safety reasons
- Refer to appendix for the list of countries where the vaccine is currently licensed
- Refer to previous submission for additional information

2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
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- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

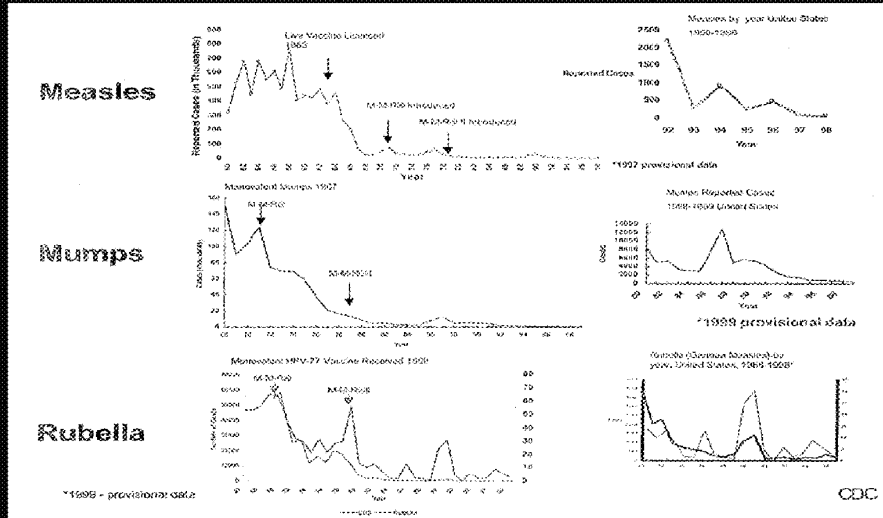
12

2.5.1.4: Scientific Background

- Highlight the clinical presentation and epidemiology of the 3 targeted diseases before vaccination and the impact of vaccination
- Provide historical perspective on monovalent and multivalent measles-mumps-rubella live attenuated vaccines (impact on the incidence of the 3 diseases, clinical presentation of vaccine-induced symptoms).
- Provide general information about M-M-R™II: Safety, Immunogenicity, and Efficacy. Impact of maternal antibodies and kinetics of antibodies to measles, mumps, and rubella.
- Explain the evolution in mumps potency (minimum immunizing dose and change in end-expiry potency from 5,000 to 20,000 TCID50/dose)

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Epidemiology of Measles, Mumps, and Rubella (U.S. 1965 – 1999)



Key Mumps Virus Potency Values

Vaccine Component	Minimum Immunizing Dose (TCID ₅₀ /dose)	End-Expiry Potency (TCID ₅₀ /dose)	Minimum Release Potency (TCID ₅₀ /dose)
REDACTED – OMP			
Mumps	~2.5 log ₁₀ (~317) [§]	3.7 log ₁₀ (5,000) [¶]	4.7 log ₁₀ (50,000) [¶]
REDACTED – OMP			
<p>[§] In 1972, potency value had to be adjusted (4-fold increase) due to a change in cell substrate (from BSC-1 to Vero cells).</p> <p>[¶] In 1999, minimum release was changed from 4.7 to 5.0 log₁₀ in agreement with CBER to support an end-expiry potency of 4.3 log₁₀ instead of 3.7 log₁₀ TCID₅₀.</p>			

2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1.5: Overview of Clinical Development Program

- State that application is to obtain approval to lower mumps end-expiry potency in M-M-R™II based on the clinical data; that lowering will reduce amount of unneeded virus given to children while preserving safety and efficacy profiles of the vaccine.
- Explain that lowering of mumps potency would more likely affect immunogenicity rather than safety
- Provide rationale for the conduct of this clinical trial (need to identify mumps end-expiry potency). What was the plan and How was it done?
- Vaccine aged at room temperature to mimic natural potency decay
- Briefly state that in agreement with CBER, study was done with oGOS as vaccine stabilizer; vaccine made with oGOS provides comparable immune responses to vaccine made with GOS (report provided in section 5.3.5)
- Describe briefly protocol 007: study objective, Rationale for evaluating the kinetics of immune responses (1 year persistence).

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Targeted and Estimated Virus Potencies of Clinical Materials used in M-M-R™II Protocol 007

M-M-R™II sublot	Antigen	Targeted Potency (log ₁₀ TCID ₅₀)	Estimated Potency (log ₁₀ TCID ₅₀)†	Adjusted Potency (log ₁₀ TCID ₅₀)‡
M-M-R™II containing ≤3.7 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	≤3.7	3.7	3.8
M-M-R™II containing ≤4.0 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	≤4.0	3.9	4.0
M-M-R™II containing ~4.9 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	~4.9	4.7	4.8

† Point estimate potency adjusted to mumps house standard value of 4.2
 ‡ Point estimate potency adjusted to mumps house standard value of 4.3

2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
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- 2.5.1.8: Good Clinical Practices

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2.5.1.6: Standard Research Procedures

- Conduct and Design of Study: Concordance with Standard Research Approaches (well-controlled, well powered, etc.)
- Vaccination Report Card (VRC)
- Similar to the one used in recent M-M-R™II studies
- Parameters prompted for on VRC and how often (Temperature, injection-site reaction, systemic AE)
- Statistical Analysis
- State that statistical analyses were pre-specified in the DAP
- Analyses performed according to standardized and validated methodology; refer section explaining methodology

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2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1.7: Regulatory Guidance and Advice

- Selection of assays used for primary immunogenicity endpoints
- Assay cutoffs – discussions with CBER
- Need to evaluate the kinetics of immune responses (1 year persistence).
- GOS and oGOS discussion
- Minutes of meetings with regulatory agencies (To be referenced)

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2.5.1: Product Development Rationale

- 2.5.1.1: Pharmacological Class
- 2.5.1.2: Chemical and Pharmaceutical Properties
- 2.5.1.3: Current and Targeted Indications
- 2.5.1.4: Scientific Background
- 2.5.1.5: Overview of Clinical Development Program
- 2.5.1.6: Standard Research Procedures
- 2.5.1.7: Regulatory Guidance and Advice
- 2.5.1.8: Good Clinical Practices

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2.5.1.8: Good Clinical Practices

- Study was conducted using Good Clinical Practice (GCP) guidelines: study design, use of appropriate controls, power, appropriateness of the delta used to compare the different groups.
- Quality assurance audited by Merck WCQAR and audits meet US and International standards.
- Parameters used to evaluate safety were in harmony with previous experiences with the product (rash, fever).
- Laboratory assays met all required standards (assays were validated).

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2.5: Clinical Overview

- 2.5.1: Product Development Rationale
- 2.5.2: Overview of Biopharmaceutics (Not Applicable)
- 2.5.3: Overview of Clinical Pharmacology (Not Applicable)
- 2.5.4: Overview of Efficacy
- 2.5.5: Overview of Safety
- 2.5.6: Benefits and Risks Conclusions
- 2.5.7: List of References

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2.5: Clinical Overview

- 2.5.1: Product Development Rationale
- 2.5.2: Overview of Biopharmaceutics
- 2.5.3: Overview of Clinical Pharmacology
- 2.5.4: Overview of Efficacy
- 2.5.5: Overview of Safety
- 2.5.6: Benefits and Risks Conclusions
- 2.5.7: List of References

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2.5 Clinical Overview

- 2.5.4: Overview of Efficacy
 - 2.5.4.1: Efficacy
 - 2.5.4.2: Immunogenicity

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BJK8

2.5.4: Overview of Efficacy

- 2.5.4.1: Efficacy
- Provide overview of the efficacy of M-M-R™II and state that efficacy was shown with monovalent products
- Provide importance of vaccine efficacy as provided by the fact that measles, mumps, and rubella (and associated complications) have been virtually eliminated from countries such as Finland, Sweden, and United States.
- Immunogenicity was shown to correlate well with efficacy.
- State that neutralization assay was used as primary immunogenicity endpoint in agreement with the regulatory

Slide 28

BJK8 Suggest first bullet say this is a "brief" summary

Change "bleeding" in last bullet to "blood specimen" - not sure how persistence fits under efficacy?

Barbara J. Kuter, 10/23/2003

2.5 Clinical Overview

- 2.5.4: Overview of Efficacy
 - 2.5.4.1: Efficacy
 - 2.5.4.2: Immunogenicity

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2.5.4: Overview of Efficacy

- 2.5.4.2: Immunogenicity
- State that 4.0 log₁₀ TCID₅₀ was satisfactory but not 3.8 log₁₀ TCID₅₀
- Indicate study hypotheses and statistical criteria for success
- Present study results by PRN then by ELISA (first 4.0 then 3.8)
- Present data related to the 1 year persistence showing that persistence was high (>95%) for all 3 antigens across treatment groups
- Conclusions on the immunogenicity: state that application supports an end-expiry dose of mumps virus in M-M-R™ to be no less than 4.0 log₁₀ TCID₅₀/dose based on the 3 key immunogenicity results (4.0 satisfactory but not 3.8; and responses persisted for at least 1 year)

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Analysis of Non-Inferiority and Acceptability of Mumps PRN Seroconversion Rates by Treatment Groups

≤4.0 log ₁₀ TCID ₅₀ Mumps Potency (N=662)			~4.8 log ₁₀ TCID ₅₀ Mumps Potency (N=672)		Estimated Difference (90% CI)	Acceptability	Similarity
n	Observed SCR (95% CI)	Estimated SCR	n	Estimated SCR			
433	93.3% (90.5%, 95.5%)	93.4%	437	92.2%	1.2 (-1.8, 4.1)	Acceptable	Similar

Analysis of Non-Inferiority and Acceptability of Mumps PRN Seroconversion Rates by Treatment Groups

≤3.8 log ₁₀ TCID ₅₀ Mumps Potency (N=663)			~4.8 log ₁₀ TCID ₅₀ Mumps Potency (N=672)		Estimated Difference (90% CI)	Acceptability	Similarity
n	Observed SCR (95% CI)	Estimated SCR	n	Estimated SCR			
459	89.3% (86.1%, 92.0%)	89.4%	437	92.2%	-2.9 (-6.1, 0.3)	Not Acceptable	Not Similar

Comparison of Antibody Responses to Me, Mu, and Ru (ELISA) (1)

Antigen	Mumps Potency (\log_{10} TCID ₅₀ /dose)				Estimated Differences (90% CI)	Non-inferiority Conclusion
	≤ 4.0 (N=662)		~ 4.8 (N=672)			
	n	Estimated SCR	n	Estimated SCR		
REDACTED – OMP						
Mumps	583	97.4%	588	98.0%	-0.6 (-2.1, 0.9)	Similar
REDACTED – OMP						

Comparison of Antibody Responses to Me, Mu, and Ru (ELISA) (2)

Antigen	Mumps Potency (\log_{10} TCID ₅₀ /dose)				Estimated Differences (90% CI)	Non-inferiority Conclusion
	≤ 3.8 (N=663)		~4.8 (N=672)			
	n	Estimated SCR	n	Estimated SCR		
REDACTED – OMP						
Mumps	577	94.1%	588	98.0%	-3.8 (-5.9, -2.0)	Not Similar
REDACTED – OMP						

2.5: Clinical Overview

- 2.5.1: Product Development Rationale
- 2.5.2: Overview of Biopharmaceutics
- 2.5.3: Overview of Clinical Pharmacology
- 2.5.4: Overview of Efficacy
- 2.5.5: Overview of Safety
- 2.5.6: Benefits and Risks Conclusions
- 2.5.7: List of References

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2.5.5: Overview of Safety

- Provide a summary of the safety results indicating comparable safety profile across treatment groups.
- State that no safety issues expected with lower potencies
- Population and Extent of exposure (how many subjects vaccinated, how many doses, how long were they followed, and mention that only vaccine-related SAEs were evaluated between day 42 and 1 year post-vaccination.)
- Explain how safety profiles were compared between each test group and the control group (risk difference)
- Provide safety results (injection site, systemic, elevated temperatures, serious AEs, death, discontinuations): All showing no significant difference across tested potencies

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2.5.5: Overview of Safety (Cont.)

- Present a summary of the safety data from end-expiry clinical trial (Comparison between test and control groups, Critical analysis of safety results, importance of safety parameters)
 - Injection site reactions
 - Systemic adverse experiences
 - Elevated temperatures
 - Deaths, Serious AEs, and Discontinuation from the study
- Limitations of Safety Data
- Worldwide Marketing Experience: 400 million doses distributed and clear impact in the incidence of the 3 diseases; vaccine generally well tolerated with favorable benefit to risk ratio to support continued usage for prevention of the 3 diseases.
- Conclusions regarding safety: data support study safety hypothesis

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Clinical Adverse Experiences Observed During 42 days Follow-up* (1)

	M-M-R™ II with Mumps ≤ 3.8 log ₁₀ TCID ₅₀ /dose		M-M-R™ II with Mumps ≤ 4.0 log ₁₀ TCID ₅₀ /dose		M-M-R™ II with Mumps -4.8 log ₁₀ TCID ₅₀ /dose	
	n	(%)	n	(%)	n	(%)
Total number of subjects	663		662		672	
Subjects with follow-up	631		636		643	
Number (%) of subjects:						
with no adverse experience	91	(14.4)	105	(16.5)	92	(14.3)
with one or more adverse experiences	540	(85.6)	531	(83.5)	551	(85.7)
MMR-related injection site reactions*	213	(33.8)	220	(34.6)	219	(34.1)
systemic adverse experiences	489	(77.5)	488	(76.7)	497	(77.3)
serious adverse experience	10	(1.6)	6	(0.9)	9	(1.4)

*Adverse experiences include those related to both M-M-R™II and Varivax, with the exception of injection site reaction

Clinical Adverse Experiences Observed During 42 days Follow-up* (2)

	M-M-R™ II with Mumps ≤ 3.8 log ₁₀ TCID ₅₀ /dose N = 631		M-M-R™ II with Mumps ≤ 4.0 log ₁₀ TCID ₅₀ /dose N = 636		M-M-R™ II with Mumps ~4.8 log ₁₀ TCID ₅₀ /dose N = 643	
	n	(%)	n	(%)	n	(%)
With vaccine-related adverse experiences	347	(55.0)	313	(49.2)	337	(52.4)
MMR-related injection-site adverse experiences*	213	(33.8)	220	(34.6)	219	(34.1)
systemic adverse experiences	181	(28.7)	148	(23.3)	150	(23.3)

*Adverse experiences include those related to both M-M-R-II and Varivax, with the exception of injection site reaction

2.5: Clinical Overview

- 2.5.1: Product Development Rationale
- 2.5.2: Overview of Biopharmaceutics
- 2.5.3: Overview of Clinical Pharmacology
- 2.5.4: Overview of Efficacy
- 2.5.5: Overview of Safety
- 2.5.6: Benefits and Risks Conclusions
- 2.5.7: List of References

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2.5.6: Benefits and Risks Conclusions

- Effectiveness and safety over the 25 years since licensure
- State that data presented in this application are consistent with historical immunogenicity and safety profiles of the vaccine, as shown with the control group receiving vaccine with mumps potency within typical release range
- Important benefit is that you can give vaccine with lower mumps potency and do not need to give more than needed

If any, possible risk would be for not giving enough mumps virus to allow protection. But study data showed that 4.0 is satisfactory and data from 3.8 is not dramatically low, therefore benefit is maintained, justifying the lowering of end-expiry potency

- Study did not change the indications and other safety parameters of the currently licensed vaccine but provides a more accurate determination of the mumps end-expiry potency, therefore will require a label change for the minimum mumps expiry potency
- Limitations of available data: sample size was not a problem

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Presentation Outline

- Module 2: Common Technical Document Summaries
 - 2.5: Clinical Overview
 - 2.7: Clinical Summary (Not required based on discussion with CBER)

- Module 5: Clinical Study Reports
 - 5.3: Clinical Study Reports
 - 5.4: Literature References

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Presentation Outline

- Module 2: Common Technical Document Summaries
 - 2.5: Clinical Overview
 - 2.7: Clinical Summary

- Module 5: Clinical Study Reports
 - 5.3: Clinical Study Reports
 - 5.4: Literature References

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5.3 Clinical Study Reports

- 5.3.1: Reports of Biopharmaceutic Studies
 - Not Applicable
- 5.3.2: Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials
 - Not Applicable
- 5.3.3: Reports of Human Pharmacokinetics (PK) Studies
 - Not Applicable
- 5.3.4: Reports of Human Pharmacodynamic (PD) Studies
 - Not Applicable

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5.3 Clinical Study Reports (Cont.)

- 5.3.5: Reports of Efficacy, Immunogenicity and Safety Studies
- Provide CSR for Protocol 007
- Provide report of the historical comparison of immunogenicity between M-M-R™II with oGOS and M-M-R™II with GOS
- 5.3.6: Reports of Post-marketing Experience
- Provide 5 year Post-marketing report (1996-2002)
- 5.3.7: Case Report Forms and Individual Subject Listings

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Presentation Outline

- Module 2: Common Technical Document Summaries
 - 2.5: Clinical Overview
 - 2.7: Clinical Summary

- Module 5: Clinical Study Reports
 - 5.3: Clinical Study Reports
 - 5.4: Literature References

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Methods Used To Achieve Expiry Potencies

M-M-R™ _{II} Sublots	Experimental Conditions
M-M-R™ _{II} containing ≤ 3.7 \log_{10} TCID ₅₀	Room Temperature for 12 weeks
M-M-R™ _{II} containing ≤ 4.0 \log_{10} TCID ₅₀	Room Temperature for 7 weeks
M-M-R™ _{II} containing ~ 4.9 \log_{10} TCID ₅₀	No Manipulation

48

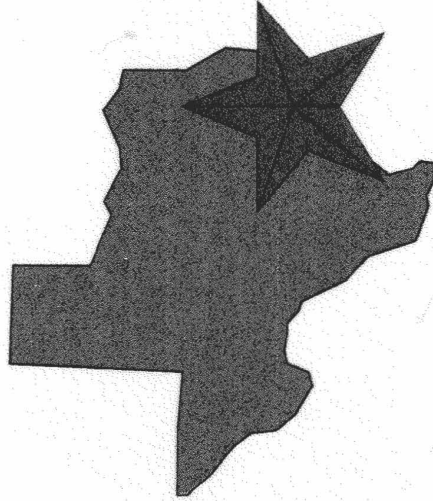
Targeted and Estimated Virus Potencies of Clinical Materials used in M-M-R™II Protocol 007

M-M-R™II sublot	Antigen	Targeted Potency (log ₁₀ TCID ₅₀)	Estimated Potency (95% CI) (log ₁₀ TCID ₅₀)†	Adjusted Potency (log ₁₀ TCID ₅₀)‡
M-M-R™II containing ≤3.7 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	≤3.7	3.66 (3.69)	3.8
M-M-R™II containing ≤4.0 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	≤4.0	3.94 (3.98)	4.0
M-M-R™II containing ~4.9 log ₁₀ TCID ₅₀	REDACTED – OMP			
	Mumps	~4.9	4.7	4.8
	REDACTED – OMP			

† Point estimate potency adjusted to mumps house standard value of 4.2
 ‡ Point estimate potency adjusted to mumps house standard value of 4.3

10/25/2019
Declaration of G. Reilly
EXHIBIT 119

M-M-RTMII EXPIRY INVESTIGATORS MEETING



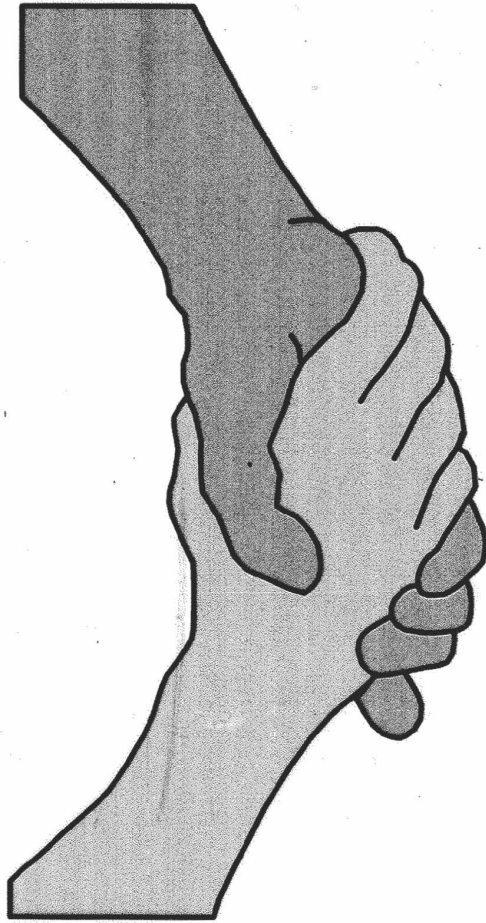
Irving, Texas

March 15-16, 1999

CONFIDENTIAL

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MRK-CHA01888826
Appx4760

INTRODUCTIONS



MERCK PERSONNEL

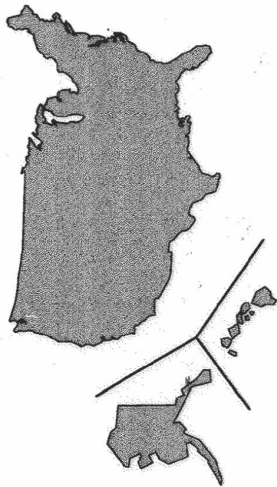
- **Clinical**
 - Megan McBride
 - Kara Stockett
 - Colleen Taddeo
 - Dr. Scott Thaler
- **Statistics**
 - Dr. Stephanie Olsen
- **Quality Assurance**
 - Susan McNeill
- **Biometrics Research**
 - Timothy Schofield
- **Virus & Cell Biology**
 - Dr. David Krah
 - Mary Yagodich
- **Data Coordination**
 - Leighann Graham
- **Merck Vaccine Division**
 - Gina Esposito
 - Kim Haupt
 - Maureen Walter

MERCK PERSONNEL (cont'd)

MRAS

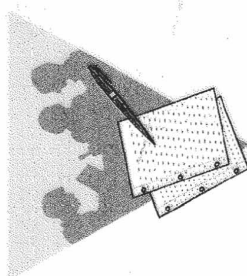
Medical Research Associates

- Yolie Amisola-Crume
- Cathy Anderson
- Joanne Bixler
- Jane Brunette
- Nicole Christison
- Michele Goldberg
- Madigan Harris
- Darrell Johnson
- Julie Kennedy
- Lee Lesneski
- John Loder
- Karen Martin
- Patricia Morgan
- Lawrence Peterson
- Nancy Reinhardt
- Jill Ryan
- John Smith
- Michelle Stallworth
- Eloise Watkins

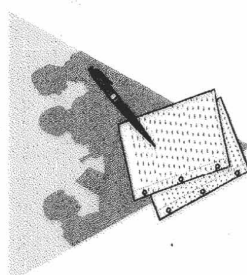


STUDY SITES

- Boston
- Buffalo
- Chapel Hill
- Dallas
- Denver
- Honolulu
- Jackson
- Marshfield
- Nashville
- Norfolk
- North Canton
- Oakland
- Pittsburgh
- Rochester
- Salt Lake City
- San Diego



AGENDA



- Introduction – Dr. Scott Thaler
- Protocol Background & Rationale – Dr. Scott Thaler
- Protocol Overview & Administrative Issues – Megan McBride / Kara Stockett
- Case Report Forms – Leighann Graham
- Handling & Shipping of Sera – Megan McBride / Kara Stockett
- Question & Answers – ALL
- LUNCH – ALL
- Adverse Event Review – Video
- Study Monitoring – Darrell Johnson
- Regulatory Aspects & Quality Assurance – Susan McNeill
- Questions & Answers – ALL
- Closing Remarks – Dr. Scott Thaler

**A Study of M-M-R™II at Mumps
Expiry Potency in Healthy
Children 12-18 Months of Age**







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MRK-CHA01888832
Appx4766

BACKGROUND AND RATIONALE

- The components of M-M-R™II are live viruses and lose potency over time when stored at 2-8°C or higher.
- The FDA (CBER) has requested expiry potencies be placed on the label of M-M-R™II.
- No data exist for mumps at the expiry potency Merck has selected.
- A clinical immunogenicity trial is necessary to provide these data.

M-M-RTM II END EXPIRY POTENCIES SUGGESTED FOR THE LABEL

<u>Component</u>	<u>Potency/Dose</u> (<u>log₁₀ TCID₅₀</u>)
	
Mumps	3.7
	

REDACTED – OMP

REDACTED – OMP

DETERMINATION OF VACCINE SHELF-LIFE

Target or Fill Potency

Vaccine Stability

Minimum Immunizing Dose

TABLE 3: Marketing Stability Results for Measles Containing Vaccines

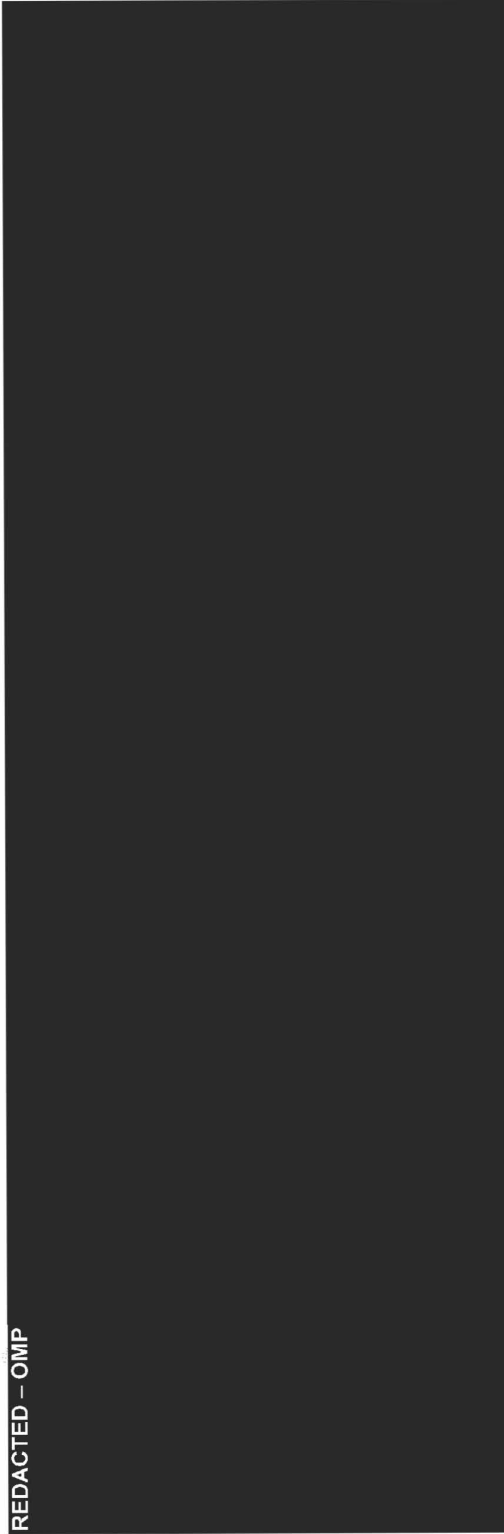


TABLE 4: Marketing Stability Results for Mumps Containing Vaccines

Lot Subset	# of Lots	Total Loss: Release to 24 Mos.			Predicted Expiry Potency at 24 Mos.		
		Average	95% LCL	95% UCL	Average	95% LCL	95% UCL
Single Dose	65	0.52	0.36	0.68	4.45	4.29	4.61
Multi-Dose	10	0.37	0.21	0.52	4.53	4.37	4.68
All	75	0.50	0.37	0.64	4.45	4.32	4.59

MEASLES AND MUMPS DATA ON MINIMUM IMMUNIZING DOSE

- Buynak EB et al. JAMA 1969; 207: 2259-62.
 - Includes data on MeMu, MeMuRu bi/trivalent
- Buynak EB et al. JAMA 1968; 203: 9-13.
 - Mu only
- Stokes J et al. Pediatrics 1967; 39: 363-71.
 - Mu only

**MINIMUM IMMUNIZING DOSE:
MEASLES DATA**

REDACTED - OMP



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MRK-CHA01888838
Appx4772

MINIMUM IMMUNIZING DOSE: MUMPS DATA

Vaccine	Dose	N	SCR	GMT (SNT)
Trivalent (HPV-77)	4.4	28	93%	8
MeMu bivalent	3.8	13	77%	5
Mu mono	3.1	11	100%	4.5
Mu mono	3.1	13	100%	7.2
Mu mono	1.6	8	75%	1.5

DETERMINATION OF MEASLES AND MUMPS SHELF LIFE

(all values in \log_{10} TCID₅₀)

	Expiry Potency	95% UL on 24 Month Loss	Target Fill	Buffer	Minimum Immunizing Dose
REDACTED – OMP					
Mumps	4.3	0.64	4.9	-0.04	3.1

PRODUCTION OF M-M-R™II AT EXPIRY

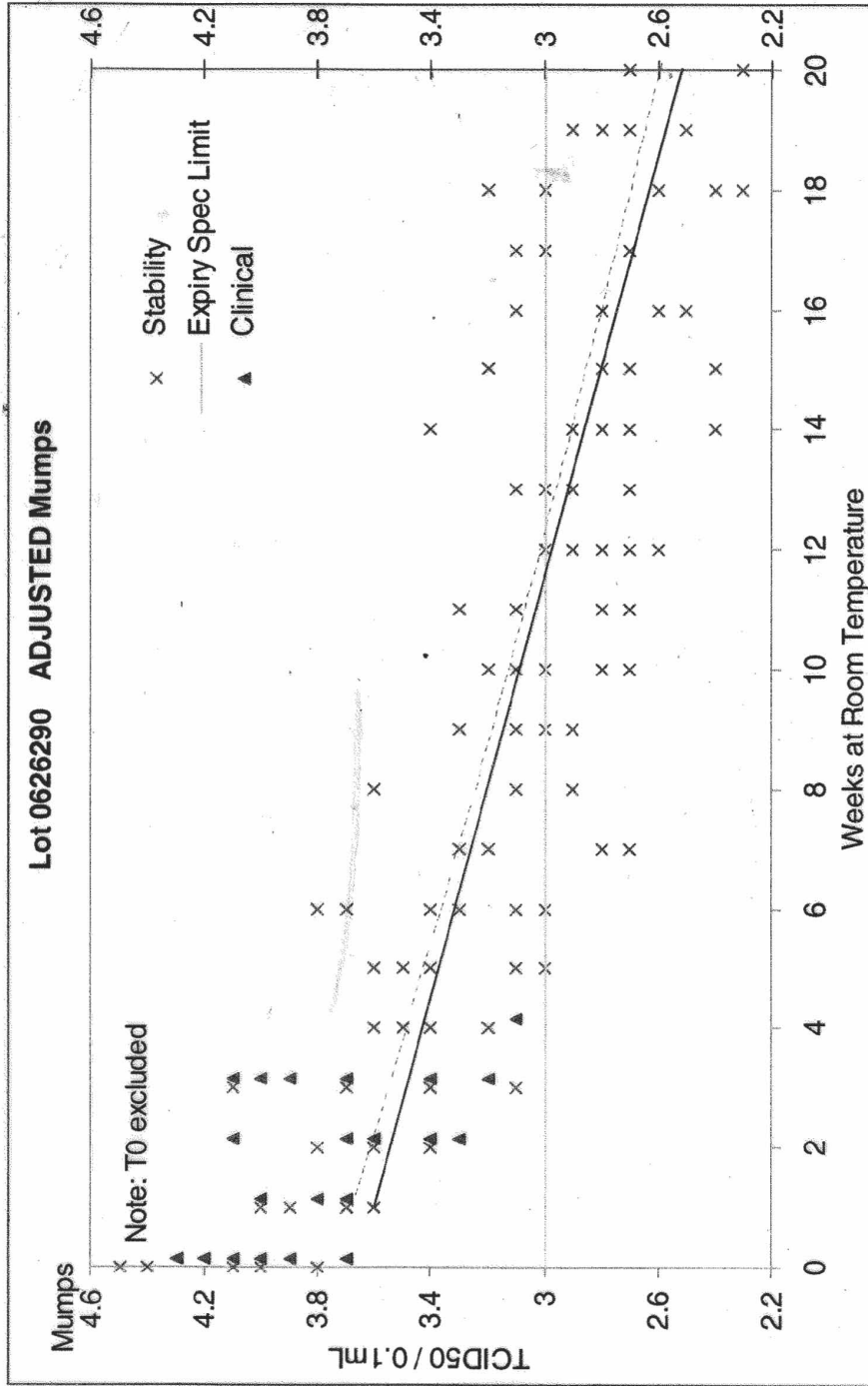
- Natural Aging (2-8°C).
- Accelerated Aging at Room Temperature (20-25°C).
- Dilution of Components.

<u>Study Type</u>	<u>Advantages</u>	<u>Disadvantages</u>
<p>Accelerated Aging at Room Temperature (20-25°C)</p>	<ul style="list-style-type: none"> • Material may be produced relatively quickly • Change in live/inactive particle ratio similar to natural aging 	<ul style="list-style-type: none"> • Heat-induced qualitative antigenic changes • Effect on all 3 viruses in M-M-R™_{II} not predictable • Effect on more susceptible sub-populations
<p>Dilution</p>	<ul style="list-style-type: none"> • Material available relatively quickly • No heat-induced change in antigenicity • Enhance theoretical interference between components • Similar effects on all sub-populations 	<ul style="list-style-type: none"> • Least similar to natural aging process • Alteration in protein concentration • Ratio of live/inactive particles not maintained
<p>Natural Aging at 2-8°C</p>	<ul style="list-style-type: none"> • Measures real-time stability and decay 	<ul style="list-style-type: none"> • Very slow process • Effect on all 3 viruses in M-M-R™_{II} not predictable

THE PRELIMINARY AGING EXPERIMENT

- **Goal:**
 - Reduce vaccine potency while minimizing the margin of error and ensure the true potency is no greater than the target.
- **Methods:**
 - Incubate 3 potential clinical lots at room temperature.
 - Use a 1x6 potency testing scheme for 27 weeks.
 - Generate best fit curves using all available data.
 - Begin aging clinical material once decay understood.

Stability Data for Lot #0626290 Showing Results of Tests on Clinical Samples for Mumps.



ESTIMATED POTENCIES OF STUDY SUBLOTS

Group	N	Measles Titer (log ₁₀ TCID ₅₀)	Mumps Titer (log ₁₀ TCID ₅₀)	Rubella Titer (log ₁₀ TCID ₅₀)
Sublot #1	500	REDACTED - OMP	~4.9	REDACTED - OMP
Sublot #2	500	REDACTED - OMP	~3.98	REDACTED - OMP
Sublot #3	500	REDACTED - OMP	~3.69	REDACTED - OMP

IMMUNOGENICITY MEASUREMENTS

REDACTED – OMP

- For Mumps, a functional (neutralization) assay has been developed.
 - Neutralization will be measured using a “bread and butter” plaque reduction neutralization (PRN) assay.
 - a wild type mumps strain will be used in the PRN assay to best assess protection from wild mumps infection.

PLAQUE REDUCTION MUMPS NEUTRALIZATION ASSAY

- Serum dilutions are mixed with TN wt mumps for one hour, quenched, then added to Vero cell monolayers:
 - Presamples to be tested at 1:2 and 1:4.
 - Postsamples to be tested at 1:4 and 1:8.
 - A randomly selected subset (~20%) will be diluted out to titer to compute GMTs.
- Incubated 6 days with media supplemented with agarose.
- Stained with 0.2% Coomassie Blue R-250 in ETOH.
- Titer is the highest dilution that leads to at least 50% plaque reduction.

PRELIMINARY GUIDELINES FOR THE PRN ASSAY

- **Negative (not protected)**
 - $<1:2$
- **Positive (protected)**
 - $\geq 1:4$
- **Seroconversion by PRN**
 - ≥ 4 fold rise in antibody titer

ADVANTAGES TO PARTICIPATION IN THIS TRIAL FOR SUBJECTS

- Avoid unnecessary exposure in the future to higher levels of mumps vaccine virus.
- A positive mumps neutralization titer almost certainly ensures protection from wild type infection.
- Lower doses of mumps may be associated with lower rates of side effects.

PROTOCOL 007



A Study of M-M-RTMII at Mumps Expiry Potency in Healthy Children 12 to 18 Months of Age

PRIMARY OBJECTIVES

- To demonstrate a similar immune response to mumps by neutralization among subjects receiving M-M-R™II containing an expiry dose of mumps compared to subjects receiving M-M-R™II containing a release dose of mumps.
- To demonstrate an adequate immune response to mumps among subjects receiving M-M-R™II with an expiry dose of mumps.

SECONDARY OBJECTIVES

- To demonstrate similar immune responses (by ELISA) for measles, mumps and rubella among children who receive M-M-RTMII containing an expiry dose of mumps and children receiving M-M-RTMII containing a release dose of mumps.
- To summarize the GMTs to measles, mumps, rubella and varicella 42 days postvaccination in both the expiry and control groups.

SECONDARY OBJECTIVES

(cont'd)

REDACTED - OMP



- To summarize the proportion of subjects with mumps PRN titers \geq 1:8 in both expiry and control groups.

SECONDARY OBJECTIVES

(cont'd)

- To summarize the PRN titers (GMTs) in a randomly selected subset of subjects in both the expiry and control groups 42 days postvaccination.
- To describe the safety and tolerability of M-M-RTMII containing an expiry dose of mumps given concomitantly with VARIVAXTM.

STUDY DESIGN SUMMARY

- Randomized, Double-Blind, Multi-Center Study
- 3 Groups:
 - **Control** ($\sim 4.9 \log_{10}$ TCID₅₀ mumps).
 - **Intermediate Expiry** ($\sim 4.0 \log_{10}$ TCID₅₀ mumps).
 - **Expiry** ($\sim 3.7 \log_{10}$ TCID₅₀ mumps).
- Each subject receives a single injection of M-M-RTMII and VARIVAXTM.
- 3 Visits: Day 0, day 42-56, and at one year.

Study Flow Chart

<u>TEST/PROCEDURE</u>	Sublot #1 M-M-R™ _{II} A (Control Group)			Sublot #2 M-M-R™ _{II} B (Mumps Expiry Group)			Sublot #3 M-M-R™ _{II} C (Mumps Expiry Group)		
	Day 0	Day 42 (42-56)	Day 365 (335-395)	Day 0	Day 42 (42-56)	Day 365 (335-395)	Day 0	Day 42 (42-56)	Day 365 (335-395)
<u>VACCINATION</u> M-M-R™ _{II}	X			X			X		
REDACTED – OMP									
<u>OBTAIN BLOOD SAMPLE</u>	X	X	X	X	X	X	X	X	X
<u>LABORATORY TESTS</u> Mumps Neutralization Assay ELISA	X	X	X	X	X	X	X	X	X
REDACTED – OMP									
<u>CLINICAL FOLLOW-UP</u>		X			X			X	

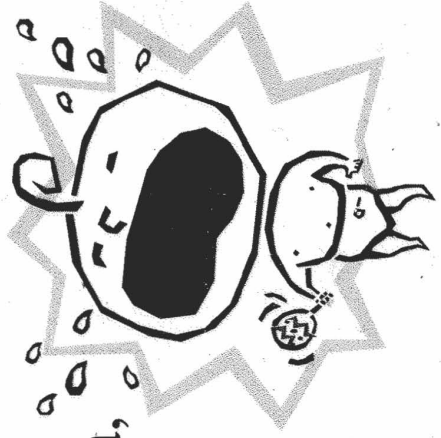
INCLUSION CRITERIA



- Children 12-18 months of age.
- In good health based on medical history.
- Signed informed consent form.
- No clinical history of vaccination for measles, mumps, rubella, varicella or zoster.

EXCLUSION CRITERIA

- Prior measles, mumps, rubella or varicella vaccine.
- Prior clinical history of measles, mumps, rubella, varicella or zoster.
- Any allergy to vaccine components including anaphylactoid allergy to eggs.
- Any exposure to measles, mumps, rubella, varicella or zoster in the past 4 weeks.



STUDY FLOW CHART

- Day 0:
 - Review Eligibility
 - Obtain History/Consent
 - Obtain Blood Sample (~5-10 mLs)
 - Administer Vaccines:
 - M-M-R™II to the Arm
 - VARIVAX™ to the Thigh
 - Hand-out and Review VRC with Parent

EXCLUSION CRITERIA

(cont'd)

- Receipt of immune globulin or blood products within 3 months of entry or 42 days thereafter.
- Febrile illness within 72 hours of vaccination.
- Any immune impairment including immunosuppressive chemotherapy.
- Vaccination with other live attenuated vaccines 30 days prior to entry or 42 days thereafter.
- Vaccination with any inactivated vaccine 14 days prior to entry or planned 42 days thereafter.

CONCURRENT TREATMENTS

- No live virus vaccine for 30 days before and 42 days after each dose of vaccine administered in this study.
- No inactivated vaccines (Hib, DTP, etc.) for 14 days before and 42 days after receipt of each dose of the vaccine.

STUDY FLOW CHART

(cont'd)

- Day 42 to 365:
 - Follow-up for vaccine-related SAEs
- Day 365 (335 to 395 days):
 - Obtain Blood Sample (~ 5-10 mLs)
 - Complete 1-year Persistence Bleed Workbook
 - Collect Exposure Information

STUDY FLOW CHART

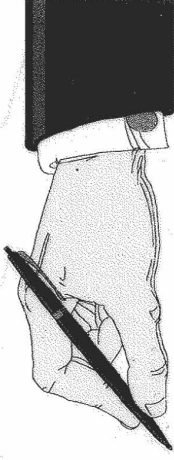
(cont'd)

- Day 0 to 42:
 - Safety Follow-up
- Day 42 (42 to 56 days):
 - Obtain Blood Sample (~5-10 mLs)
 - Collect VRC and Review
 - Collect Exposure Information
- Day 279 (9 months Post-Vaccination):
 - Telephone Contact with Parent

ALLOCATION NUMBERS

- Assign allocation number after subject is consented, inclusion/exclusion criteria are reviewed, and pre-vaccination blood draw is performed.
- A baseline number will only be assigned if the subject is consented but the vaccination does not occur. Contact MPC for assignment of baseline number.

CONSENT



-
- Investigator must obtain written consent from each potential subject's parent/guardian prior to performing any clinical research procedures.
 - Parent/guardian must sign two copies:
 - *One signed copy for study files.
 - *One signed copy for parent/guardian.

CONCURRENT TREATMENTS

(cont'd)

- No administration of immune globulin or blood products for 3 months (90 days) before or 42 days after vaccination unless there is a medical emergency warranting their use.
- No salicylates during the 6 weeks after vaccination because the use of salicylates in children with varicella has been associated with Reye's syndrome.

BLINDING (cont'd)

- Sites will unblind a subject only in the event of a **medical emergency.**
- Masked Schedules for unblinding subjects will be maintained with the SPONSOR and at the primary site.
- Masked Schedules should be maintained in a secure location.
- At the end of the study, all masked schedules should be returned to the SPONSOR either intact or with the unblinding log.

BLINDING

- The following persons will be blinded until all subjects have completed the study and data is screened for completeness:
 - SPONSOR personnel directly involved in study.
 - Subject/Parent/Guardians.
 - Investigators.
- All vials of M-M-R™II will appear identical.
- Any vial of *supplied* VARIVAX™ may be used.

SUGGESTED METHOD FOR BLOOD COLLECTION

- Blood should be drawn (~ 5-10 mLs).
- Blood should be allowed to clot in the collection tube for 30-60 minutes.
- Clotted blood should not sit at room temperature or refrigerated for more than 2 hours before centrifugation and separation.
- Do not refrigerate newly collected blood.
- After separation place the serum in a vial provided by Merck and place the correct label on the vial prior to freezing. Use only Merck provided vials and labels.

SERUM VIAL LABELS

Label Color

Bleed Interval

Red

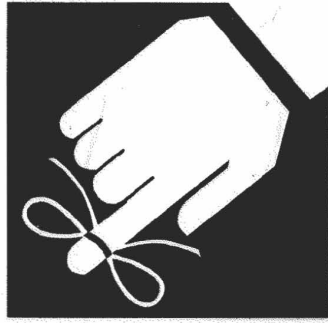
PRE

Blue

Day 42

Yellow

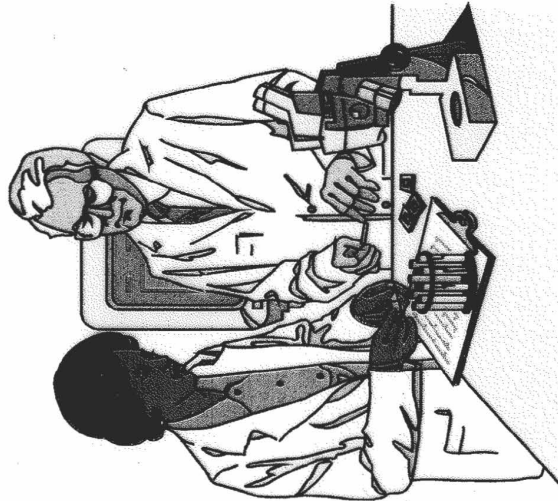
1-Year



REMINDER



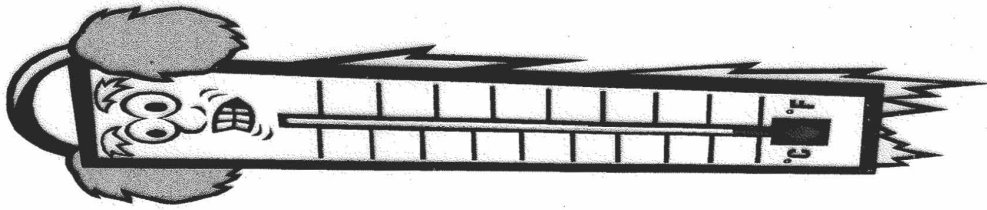
- Kyna:
Serum Samples
- Megan or Kara:
CRFs and
Correspondence



VACCINE SHIPPING AND STORAGE

- Because the M-M-RTMII in this trial is artificially aged, all M-M-RTMII vaccine will be shipped and stored frozen at -15°C.
- **REDACTED - OMP**
- For consistency, both M-M-RTMII and VARIVAXTM should be used within 30 minutes of reconstitution.

STORAGE OF VACCINE



- M-M-R™II / VARIVAX™
 - 15°C (+5°F) or colder, frost-free freezer.
- All vaccines supplied in 0.7 mL vials for a 0.5 mL injection.
- The vaccines must be administered within 30 minutes.
- Daily monitoring and documentation must be maintained for freezers and refrigerators.

STORAGE OF DILUENT

- 2 to 8°C (36 to 46°F) or room temperature.
- Supplied in 0.7 mL vials.
- For use with M-M-R™II and VARIVAX™.

RETENTION VIALS

- Use to monitor shipping, handling and storage of vaccines.
- 12 Vials of each vaccine (M-M-R™II, VARIVAX™) designated as retention vials.
- Must be stored with the study vaccine but not used during the trial.
- Must be returned to SPONSOR within 3 months of study completion or as requested.

REPLACEMENT VIALS

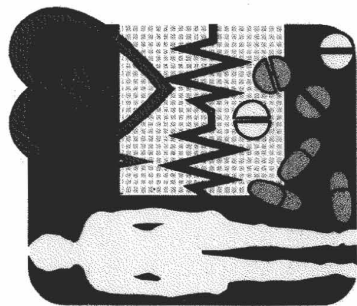
- Replacement vials will be available at each site to be used in the event of an error in reconstitution of vaccine or if not administered within 30 minutes.
- Contact MPC or Monitor (at home if needed) for replacement number.

ADVERSE EXPERIENCE

(AE)

“Any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with any use of a Merck product in humans.”

Whether or not considered related to the use of the product



ADVERSE EXPERIENCES

AE

NO

Pre-existing condition

YES

RECURRENCE/WORSENING

of a pre-existing condition

CLASSIFYING AEs BY INTENSITY

Mild:

- Awareness of symptom, but easily tolerated.

Moderate:

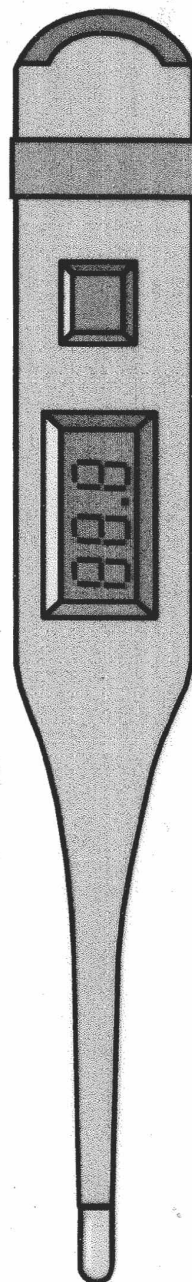
- Definitely acting like something is wrong.

Severe:

- Extremely distressed or unable to do usual activities.

SAFETY MEASUREMENTS

- All AEs, whether systemic or injection-site occurring 42 days after each injection must be reported.
- Parent/guardian will record numerical temperatures for 42 days after each injection.



SAFETY MONITORING



Report to Merck within 24 hours:

- All serious adverse experiences occurring 42 days after each injection.
- Only vaccine-related SAEs after Day 42 through Day 365.

SERIOUS ADVERSE EVENTS

- Is life threatening.
- Results in a persistent or significant disability or incapacity.
- Results in or prolongs an existing in-patient hospitalization.
- Is a congenital anomaly or birth defect.
- Is cancer.
- Is the result of an overdose.
- Other important medical event .
– (ex. Febrile seizures)



AES MUST BE REPORTED

- Serious AEs - within 24 hours to one of the individuals listed on the SPONSOR contact page of the protocol (usually via MPC):
 - Megan McBride ☎ (610) 397-2941
 - Kara Stockett ☎ (610) 397-2207
 - Scott Thaler, M.D. ☎ (610) 397-2625
- All AEs are to be recorded on case report forms.

RASHES

- Measles or rubella-like and/or varicella-like rashes should be seen by study physician.
- Exposure to measles, mumps, rubella, varicella or zoster should be documented on the appropriate CRF.

RASHES

(cont'd)

- If a child is thought to have measles, rubella, measles or rubella-like rash, mumps, mumps-like symptoms, varicella, varicella-like rash or zoster:
- Collect exposure information and complete appropriate CRFs.



STUDY DURATION

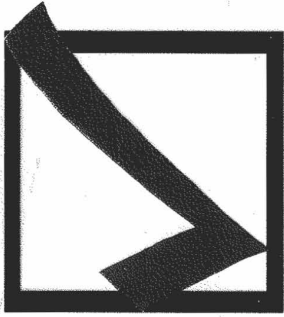
- Subject has completed study if:
- 42 days of safety follow-up after each vaccination.
- Received all scheduled vaccinations, and
- Pre- and Post-vaccination serum samples obtained.

CONFIDENTIALITY

- By signing the protocol the investigator affirms that information furnished by MRL will be maintained in confidence.
- Information will be provided to the IRB; affiliated institution; and employees only under the understanding of confidentiality.
- Records must be maintained in a secure location.

PUBLICATIONS

- We will establish a publications committee during the trial.
- MRL must review all publications 60 days prior to submission.
- Information identified by MRL as confidential must be deleted from any publication.



IRB APPROVAL

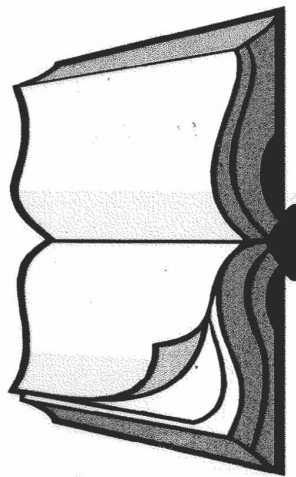
Written approval from the IRB must be forwarded to MRL before clinical supplies will be shipped. For continuing studies, written approval from the IRB must be sent to MRL at intervals not to exceed one year.

STUDY REQUIREMENTS

- IRB approval of protocol/consents.
- FDA 1572 Form.
- Signed Protocol/Completed Title Page.
- Copy of approved consent forms.
- CVs for all personnel working on study.
- Pre-study site visit (Merck MRA).
- IRB Compliance Letter

ADMINISTRATIVE BINDER

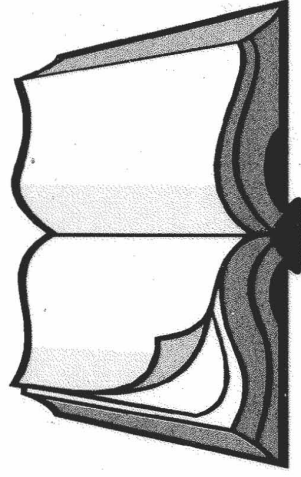
- Merck Contacts.
- Protocol/Amendments.
- Consent Form.
- IRB Approval.
- Personnel Signature Page.
- Allocation Numbers/Study Enrollment Log.



ADMINISTRATIVE BINDER

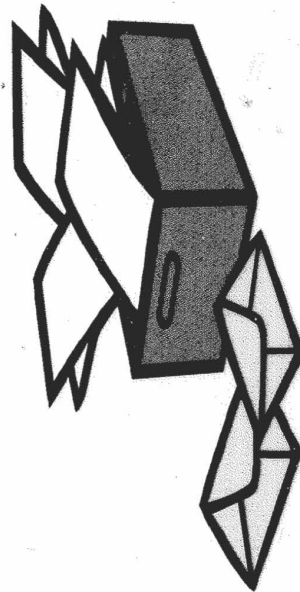
(cont'd)

- Data Collection Forms/Instructions.
- Vaccine Storage/Temperature Log.
- Vaccine Accountability>Returns.
- Good Clinical Practices.
- Serious AEs.
- Merck Monitoring Log.
- Correspondence.



RECORDS RETENTION

Government agency regulations and directives require documentation pertaining to a clinical trial must be retained by the investigator for a minimum of 2-years after notification by MRL, or longer if requested by MRL.



MEDICAL PROGRAM COORDINATOR

- Administrator for Merck Clinical Trials.
- Primary contact for study information.
 - *Serious Adverse Experiences*
- Responsible for study initiation, data collection and review.
- Summarization of study findings.



MERCK CONTACTS

Clinical Monitor

Scott Thaler, M.D.

 (610) 397-2625

FAX (610) 397-3371

Medical Program Coordinators

Megan McBride  (610) 397-2941

FAX (610) 397-3371

Kara Stockett  (610) 397-2207

FAX (610) 834-7555

HANDLING AND SHIPPING OF SERA

Presenters:

Megan McBride and Kara Stockett

AGENDA

- Supplies received from Merck
- Checklist for shipping serum samples
- Packaging and shipping demonstration
- Federal Express Form
- Investigator memo

**SUPPLIES RECEIVED
FROM MERCK (via MPC)**

- Serum Vials
- Barcoded Labels for Vials
- Cell Boxes
- Shipping Boxes
- Shipping Labels (as needed)

CHECKLIST FOR SHIPPING VACCINE SERA SAMPLES

VIALS

- All samples **MUST** be in standard Merck-provided vials.
- Vials should not be overfilled (sera expands with freezing).
- Caps on vials must be tight to prevent leakage.
- All sera (not whole blood) must be frozen at the time of shipment
- Do not use parafilm or any other sealing device on Merck vials.

LABELS

- Use only Merck-provided barcoded labels on the sample vials

** If the *correct* label for a specific sample is not available *do not use any other barcoded label -- each barcode refers specifically to one sample*. Print the following information on the vial with a non water-based writing utensil: **V# Study# Case# Bleed Date Patient Initials Bleed Interval**

- No other non-Merck labels should be affixed on top of the barcoded labels

LABELS (contd.)

- Only initials and sample date are to be written on barcoded labels.
- Use indelible ink to write on labels.
- ***DO NOT use correction fluid***
- ***DO NOT*** write over or change any bar-coded information (Case #, Study #, etc.)
Each barcode is unique in the database and specific to that particular sample.

LABELS (contd.)

- Labels should be affixed so sample volumes may be seen and barcodes appear horizontally on vials.
- Date format on labels must match the date format on **IN** sheet (**MM/DD/YY** or **DD/MM/YY**).
- If the bar-coded labels do not adhere to the sample vial for any reason, affix with one strip of clear tape so that the barcode is clear and legible.

INVENTORY LIST (IN Form)

- Include white & yellow copies of IN sheet in each shipment
Retain pink copy of the IN form at the site.
Samples will not be inventoried if they are not accompanied by a completed IN form.
- List Case #, Bleed Interval, & Bleed Date on the IN form for each sample.
Samples will not be inventoried without being listed on the IN sheet along with the bleed interval and bleed date.

INVENTORY LIST (contd.)

- **SAMPLES ARE TO BE PLACED IN THE CELL BOXES IN THE SAME ORDER AS THEY ARE LISTED ON THE IN FORM.**

This is critical in order to expedite the movement of samples and ultimately to obtain assay results.

- All comments/error corrections on **IN** form must be initialed and dated.

54 CELL BOXES (for storage of serum vials)

- Order of samples in cell box must match order in which they are listed on the **IN** form.
- Vials must be upright in cell boxes.
- When full, cell box must be secured shut (rubber band or tape) so that all vials will remain in the cell box in transit

SHIPPING BOXES

- Sufficient dry ice must be included to keep samples frozen & hold cell box securely.
 - Use 10 lbs (~4.5 kg) of dry ice
- On outside of shipping box, write:
 - Investigator name
 - Vaccine Name (M-M-R™II)
 - Study number (007-XXXX)

SHIPPING BOXES (contd.)

- Shipping container must be marked or labeled “**KEEP FROZEN at -20°C**”.
- Place **Dry Ice stickers** on outside of shipping container. Dry Ice is a dangerous good but it does not require a *Dangerous Goods Shippers Declaration form*. Use a regular **FEDEX** shipping form and check the box that asks whether Dry Ice is contained in the shipment.
- IATA regulations require a **BIOHAZARD** label to be placed on the outside of any shipment which contains biological specimens. This does not signify that the samples are infectious.

GENERAL

- Serum samples should be shipped only on Mondays or Tuesdays by overnight express mail (Federal Express).
- Notify the MPC prior to shipping out and give the following information:
V#, Study #, # of samples, and # of shipping containers/boxes.
- Do not send any CRFs or other correspondence with the **IN** form and samples.

ADDRESS FOR SHIPMENT OF SERA

Ms. Kyna De Horsey
Asst. Medical Program Coordinator
Merck Research Laboratories
Building 26 Research Stockroom
Sumneytown Pike
West Point, PA 19486 USA

Telephone: (215) 652-0925

Facsimile: (215) 652-6314

PACKAGING & SHIPPING OF DIAGNOSTIC SAMPLES

(Based on IATA Packing Instructions 650)

INNER PACKAGING

- Leak-proof primary receptacle (Merck standard tubes) where the maximum quantity of substance does not exceed 100 mL.
- Compartmentalized containers for multiple primary receptacles (Merck standard cell boxes) to prevent contact and/or breakage.
- Absorbent material (durasorb pads) between primary and secondary packaging.
- Leak-proof secondary packaging (plastic bag) where the maximum quantity of substance does not exceed 500 mL.

PACKAGING & SHIPPING OF DIAGNOSTIC SAMPLES

OUTER PACKAGING

- Must be of adequate strength
- Mark “Diagnostic Specimen” or “Non-infectious Clinical Samples”
- Label with orange “Biohazard” sticker (OSHA standard)

PACKAGING & SHIPPING OF DIAGNOSTIC SAMPLES

DRY ICE

- Dry Ice is a dangerous good in and of itself, but it should **NOT** be marked as a dangerous good when used as a refrigerant in the transport of clinical samples.
- On Fedex Form, Check “Dry Ice”
(Shippers’ Declaration not required)
- Place “Dry Ice” label on outside of shipping container

SUMMARY

- Attention to detail prior to shipment of sera will result in less time spent resolving data issues later
- Sera cannot be delivered to assay lab at Merck until all data issues are resolved
- Make sure all personnel involved in handling sera are adequately trained

10/25/2019
Declaration of G. Reilly
EXHIBIT 120

To: Simon, Keiko[simonkei@NorthAmerica.msx.merck.com]
Cc: Krah, David[Krahda@NorthAmerica.msx.merck.com]; Byrnes, Vera D.[BYRNESV@NorthAmerica.msx.merck.com]; Staub, Joan M.[STAUBJ@NorthAmerica.msx.merck.com]; Arena, Deitra E.[loydei@NorthAmerica.msx.merck.com]; Yagodich, Mary[Yagodichm@NorthAmerica.msx.merck.com]; Shaw, Alan[Shawal@NorthAmerica.msx.merck.com]
From: Arena, Deitra E.
Sent: Fri 6/16/2000 12:46:37 PM
Importance: High
Subject: Backgrounder for CAS, 6/20/00
[MPS Nt backgrounder for June 20 CAS.doc](#)
[June CAS Table 3.xls](#)
[June CAS Table 4.xls](#)
[June CAS Table 5.xls](#)
[June CAS, Table 6.doc](#)
[June CAS, Table 7.doc](#)
[Microsoft Word - MPS Nt backgrounder for June 20 CAS.pdf](#)

Keiko,
Attached is the Background document for CAS in pdf format.
Deitra

From: Krah, David
Sent: Friday, June 16, 2000 8:06 AM
To: Staub, Joan M.; Arena, Deitra E.; Yagodich, Mary; Shaw, Alan
Subject: REvised MPS Nt backgrounder for CAS

All,
Attached is a re-revised backgrounder for the MPS Nt presentation to CAS. I had reversed some of the discussion on different viruses (tables 3 and 4)-These are now correct.

Thanks,
Dave

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MRK-KRA00026466
MRK-CHA00026466

Appx4849

Pilot Study of Mumps Nt Titers for Pediatric Sera

TABLE 4

Serum	Nt Titer	Against Indicator	Mumps
Sample	Vaccine	JL135 p8	LO1
484	1024	1024	128
152	512	256	64
211	256	256	32
38	512	128	16
67	512	256	256
207	256	128	16
216	256	128	32
131	512	256	32
132	256	64	64
135	256	64	64
224	256	128	32
267	256	128	64
419	512	256	512
422	512	<64	32
456	256	<64	32
514	128	256	32
3	128	64	64
129	128	64	64
138	128	64	32
519	128	128	64
237	128	256	16
264	128	64	32
265	128	64	32

MKY/DK 5/5/00

Comparison of Mumps N₁ Titers for Adult Sera Using different Indicator Viruses

TABLE 3

Neutralization titer against mumps indicator virus

Serum	Barnes	TN	Lo1	JL-135	JL-vaccine
MKY	<2, 8, 8	nd, 8, 8	nd, 8, 16	4, 16, 16	2, 8, 4
DK	<2, nd, nd	nd, nd, nd	nd, nd, nd	4, nd, nd	2, nd, nd
AS	32, 32, 64	nd, 32, 64	nd, 64, 64	64, 128, 64	64, 64, 128
CM	<32, 32, 64	nd, 64, 64	nd, 32, 64	128, 128, 256	128, 256, 128
PK	32, 32, 32	nd, 32, 32	nd, 64, 64	128, 256, 256	128, 128, 128
DW	512, 256, 256	nd, 512, 1024	nd, 512, 512	1024, 1024, 1024	1024, 1024, 1024

ND = not tested

DK 8June 2000

Mumps Plaque-Reduction Neutralization Assay Development Update
Backgrounder

June 20, 2000 CAS presentation

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MRK-KRA00026469
MRK-CHA00026469

Appx4852

I. Executive Summary

A plaque-reduction neutralization assay using a low-passage Jeryl Lynn™ preparation is being optimized for use in evaluation of sera from the M-M-R®II Expiry Trial, with a goal of providing an assay that permits measurement of a $\geq 95\%$ seroconversion rate. The low-passage Jeryl Lynn™ virus has provided neutralization titers closest to those obtained using the vaccine-passage Jeryl Lynn™, and plaques are visualized by immunostaining. Optimization of the concentration of anti-human IgG for enhancement of the neutralization is underway. The utility of the Spearman-Kärber method to calculate titers is also being considered as a final refinement to maximize the capacity of the assay to detect seroconversions.

II. Background and status of assay development

A need for a mumps neutralization (Nt) assay utilizing a wild-type indicator virus has been identified to support analysis of the immune responses to mumps in the ongoing M-M-R®II Expiry Trial (Protocol 007). Efforts to date have focused on evaluating conditions that affect assay sensitivity and in defining a suitable indicator virus in a multi-well plate plaque-reduction neutralization assay (PRN).

A summary of the mumps strains and some of the virus growth and assay parameters evaluated is presented in Table 1. Previous studies comparing neutralization titers to sera from adult lab volunteers (who had either wild-type infections or mumps vaccine-induced responses) and pediatric sera showed an effect of the virus strain on neutralization titers, with the highest seroconversion rates and titers observed for the vaccine-passage of Jeryl Lynn™ mumps. CBER has indicated that the vaccine passage Jeryl Lynn™ is not suitable for use in the PRN and has established a requirement to use a "wild-type" mumps strain to evaluate vaccine-induced immune responses. A range of wild-type isolates were therefore obtained and evaluated in the PRN to identify the optimum indicator strain. In early testing, the Tennessee (TN) isolate provided Nt titers close to those obtained using Jeryl Lynn™, but further evaluation of this strain was aborted due to difficulties in reliably detecting plaques. Several plaque staining methods were evaluated, including Coomassie Blue (general cell stain) and neutral red or tetrazolium salts (vital stains), without consistent success.

In addition to "mechanical" aspects of the assay (incubation times and temperatures, virus attachment times), two supplements were evaluated for their capacity to increase the Nt sensitivity. Complement supplementation provided modest titer increases for adult sera and was complicated by the anti-mumps activity of the complement sera. Further evaluation of this reagent was therefore not pursued. A second supplement, anti-human Ig, was evaluated to confirm its ability to increase Nt titers (approximately 100-fold titer increases), but was not immediately pursued.

Subsequent studies shifted to use the London 1 strain (Lo1) of mumps, which was also used in studies performed at CBER. This strain met the criterion of being a "wild-type" virus and became the "virus of choice" for development of

the PRN. Results of a series of pilot PRN assays of pediatric sera against Jeryl Lynn™, Lo1 and JL2 mumps strains showed respective seroconversion rates of 91% (63/69), 69% (43/62) and 56% (18/32). Testing of 169 paired sera from Protocol 006 (Competitive Trial) confirmed that the general assay format using Lo1 mumps would not provide the targeted $\geq 95\%$ seroconversion rate.

In parallel with the studies of Lo1 mumps, a sample of SBL-1 mumps (reportedly antigenically similar to Jeryl Lynn™) was obtained and evaluated in the PRN assay. SBL-1 mumps did not provide increased Nt performance versus Lo1 using a panel of pediatric and adult sera (Table 2).

Through discussion with CBER staff, the following suggestions and comments were made for evaluation in increasing the sensitivity of the PRN:

- The use of "Low-passage" JL (between passages 7 and 12) would be acceptable
- Consider assay format used by Dr. Bagher Forghani (the State of California Department of Health Services) that reportedly provides $>90\%$ seroconversion rates
 - Immunostaining (distinct "plaques" observed 3 days post-infection for all mumps strains tested in our hands).
 - Assay performed in 48-well plates
 - Evaluate the Barnes strain of mumps
- Consider using anti-human IgG to enhance Nt sensitivity
- Consider using the Spearman-Kärber method to calculate Nt titers

In response to these suggestions, stocks of the Barnes and low-passage Jeryl Lynn™ (lot 135 [passage 7], used at passage 8 in PRN assays) were obtained and evaluated in the PRN. Due to the low-cytolytic activity of these viruses, immunostaining (polyclonal goat anti-mumps antibody, peroxidase-labeled anti-goat IgG and peroxidase substrate) was adopted for detection of plaques. The immunostaining method was found to be universally applicable to detect mumps plaques (for all available strains), and therefore also permitted re-evaluation of previous strains such as TN. The 48- and 24-well plate formats (as alternatives to the 12-well plate format used in our previous studies) proved to be technically inconvenient for sample inoculation and were not pursued further.

Results of preliminary Nt assays using vaccine-passage ("house standard") and low-passage (lot 135, passage 8) Jeryl Lynn™ mumps showed that Nt titers for adult lab volunteer sera using these indicator viruses were comparable (Table 3). A series of assays was done using adult lab volunteer sera and Barnes, TN, Lo1, low-passage (lot 135, P8) Jeryl Lynn™ and vaccine passage Jeryl Lynn™ mumps as indicator viruses to determine the relative Nt for the different viruses (Table 4). Nt titers to the low-passage lot 135 Jeryl Lynn™ mumps were comparable to those obtained using the vaccine-passage virus, and greater by 2-4-fold than those to Lo1, TN or Barnes mumps. TN and Lo1 titers were comparable and approximately 2-fold higher than those to the Barnes strain of mumps. Screening of a panel of 23 pediatric sera (selected to have a titer ≥ 128 to permit assay using small serum volumes) showed that Nt titers to the vaccine-passage virus were approximately 2-fold higher than those to the low-passage

Jeryl Lynn™ and approximately 4-fold higher than those to Lo1. The low-passage Jeryl Lynn™ virus therefore provides Nt sensitivity most close to the vaccine-passage virus.

The use of the Spearman-Karber method to interpolate titers is expected to provide an increased number of seroconversions, but not to the targeted $\geq 95\%$ value. It is therefore expected that further enhancement of Nt by addition of anti-human IgG will be required. Previous studies demonstrated that this enhancement boosted post-vaccination titers approximately 100-fold, but the effect on pre-vaccination titers was not measured. In pilot studies, undiluted anti-human IgG provided positive titers to 75% of the pre-vaccination sera (9/12: titers ranging from 32 to 128) and 8-64-fold increases in post-vaccination titers, while lower amounts (1:2, 1:4 or 1:8 dilutions) of anti-IgG provided comparable enhancement of post-vaccination titers, but retained negative titers for 3/3 pre-vaccination sera (Table 5). The use of 1:4 or 1:8 dilutions of anti-IgG in a second study retained negative Nt responses for pre-vaccination sera (tested at an initial 1:32 dilution), and provided increases in titers for all three post-vaccination sera (Table 6). Results of a third experiment, using sera that previously provided titers of <2, 2 or 4, showed that a 1:2 dilution of anti-IgG permitted measurement of titer enhancements for all post-vaccination sera (Table 7). The amount of anti-IgG used in this study also resulted in positive Nt responses for several of the pre-vaccination sera. Current studies are focusing on determining the optimum concentration of anti-IgG to boost post-vaccination titers but not shift pre-vaccination sera to a positive Nt response.

III. Path forward

The proposed assay format will include:

- 12-well plate format
- Low-passage Jeryl Lynn™ indicator virus
- Enhancement of Nt with anti-human IgG
- Detection of plaques by immunostaining
- Calculation of Nt titers by 50% cutoff or Spearman-Karber method

Current studies (4-5 weeks) are designed to determine the optimum amount of anti-IgG for Nt enhancement while retaining negative titers for pre-vaccination sera. An evaluation can then be made of the effect of using the "50% Nt" cutoff (highest tested dilution tested that provides $\geq 50\%$ Nt) versus the Spearman-Karber titer interpolation to finalize the assay format. It is proposed that the optimized assay format will then be applied to the sera from Protocol 006 (4 weeks after finalization of the assay format) to provide an estimate of the seroconversion rates detected.

Issues remaining to be addressed include:

- Serum dilutions to be tested
 - the assay produces a "prozone" effect at dilutions approximately ≤ 32

-post-vaccination titers are expected to be increased approximately 100-fold

- Impact if a significant proportion of pre-vaccination sera register as Nt positive
- Impact if testing of "pre-evaluation" panel provides <95% seroconversion
- Transfer of the optimized assay

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**MRK-KRA00026473
MRK-CHA00026473**

Appx4856

Table 1

Factors evaluated for effects on Mumps Nt sensitivity

- Indicator virus
 - Jeryl Lynn™
 - Swiss isolates
 - NY
 - TN
 - SA
 - Jones
 - Enders
 - Lo1
 - JL2
 - JL5
 - SBL-1
 - Barnes
 - Select viruses passaged in CEF vs Vero (Lo1, TN, Enders, Jones)
- Incubation time and temperature of virus and serum
- Virus concentration
- Virus harvest fractions and clarification methods
- Cell substrate for virus stock growth
- Staining method for plaque visualization
(Coomassie Blue, neutral red, tetrazolium salts, immunostaining)
- Virus attachment time
- Enhancements to Nt
 - Complement (≤ 8 -fold enhancement)
 - anti-human IgG (~100-fold enhancement)

Table 2
Evaluation of PRN Titers Using Jeryl Lynn™, Lo1 and SBL-1 Mumps Strains

<u>Serum</u>	<u>Nt titer using</u>		
	<u>Jeryl Lynn™</u>	<u>Lo1</u>	<u>SBL-1</u>
1 pre	<8	<8	<8
1 post	16	<8	8
2 pre	<8	16	<8
2 post	16	8	<8
3 pre	not tested		
3 post	<8	<8	<8
4 pre	not tested		
4 post	8	8	<8
5 pre	not tested		
5 post	16	8	<8
6 pre	<8	<8	<8
6 post	16	32	<8
7 pre	<8	<8	<8
7 post	<8	<8	<8
8 pre	<8	<8	<8
8 post	16	16	<8
Adult control 1	≥128	32	16
Adult control 2	16	16	4
Adult control 3	1024	512	256

Comparison of Mumps Nt Titers for Adult Sera Using different Indicator Viruses

TABLE 3

Neutralization titer against mumps indicator virus

Serum	Barnes	TN	Lo1	JL-135	JL-vaccine
MKY	<2, 8, 8	nd, 8, 8	nd, 8, 16	4, 16, 16	2, 8, 4
DK	<2, nd, nd	nd, nd, nd	nd, nd, nd	4, nd, nd	2, nd, nd
AS	32, 32, 64	nd, 32, 64	nd, 64, 64	64, 128, 64	64, 64, 128
CM	<32, 32, 64	nd, 64, 64	nd, 32, 64	128, 128, 256	128, 256, 128
PK	32, 32, 32	nd, 32, 32	nd, 64, 64	128, 256, 256	128, 128, 128
DW	512, 256, 256	nd, 512, 1024	nd, 512, 512	1024, 1024, 1024	1024, 1024, 1024

ND = not tested

DK 8June 2000

Pilot Study of Mumps Nt Titers for Pediatric Sera

TABLE 4

Serum Sample	Nt Titer Against Indicator Mumps		
	<u>Vaccine</u>	<u>JL135 p8</u>	<u>LO1</u>
484	1024	1024	128
152	512	256	64
211	256	256	32
38	512	128	16
67	512	256	256
207	256	128	16
216	256	128	32
131	512	256	32
132	256	64	64
135	256	64	64
224	256	128	32
267	256	128	64
419	512	256	512
422	512	<64	32
456	256	<64	32
514	128	256	32
3	128	64	64
129	128	64	64
138	128	64	32
519	128	128	64
237	128	256	16
264	128	64	32
265	128	64	32

MKY/DK 5/5/00

CONFIDENTIAL

MRK-KRA00026477
MRK-CHA00026477

Appx4860

Effect of Anti-Human IgG Treatment on Mumps Nt Titers

TABLE 5

<u>sample #</u>	<u>anti human IgG dil</u>	<u>Pre serum</u>	<u>Post Seru</u>
		<u>Nt titer</u>	<u>Nt titer</u>
238	undiluted	128	>=2048
238	1:2	128	>=2048
238	1:4	256	>=2048
238	1:8	256	>=2048
238	mock anti IgG	<32	32
321	undiluted	32	>=2048
321	1:2	<32	>=2048
321	1:4	<32	>=2048
321	1:8	<32	>=2048
321	mock anti IgG	<32	32
455	undiluted	32	>=2048
455	1:2	<32	>=2048
455	1:4	<32	>=2048
455	1:8	<32	>=2048
455	mock anti IgG	<32	32

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Table 6
Enhancement of Mumps Neutralization with Anti-Human IgG

Serum #	Nt titer to Pre-serum at anti-IgG				Nt titer to Post-serum at anti-IgG			
	<u>1:4*</u>	<u>1:8*</u>	<u>Mock*</u>	<u>Historical</u>	<u>1:4</u>	<u>1:8</u>	<u>Mock</u>	<u>Historical</u>
98	<32	<32	<32	<2	≥4096	≥4096	<32	32
99	<32	<32	<32	<2	2048	2048	<32	8
101	<32	<32	<32	<2	2048	2048	128	128

* = dilution of anti-human IgG

Nt titers with anti-IgG = using Low passage Jeryl Lynn™

Historical titer = using Jeryl Lynn™ vaccine passage without anti-IgG treatment

DK 15 June 2000

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Table 7
Enhancement of Mumps Neutralization Using Anti-Human
 IgG

<u>Serum</u> ¹	<u>Nt titer to low-passage Jeryl Lynn™</u>				<u>Nt titer² to Jeryl Lynn™</u>	
	<u>Pre + anti-IgG³</u>	<u>Pre + PBS</u>	<u>Post + anti-IgG</u>	<u>Post + PBS</u>	<u>Pre</u>	<u>Post</u>
147	32	<16	≥512	<16	<2	<2
291	<16	<16	256	<16	<2	<2
4	≥64	<16	≥512	<16	<2	2
80	<16	<16	128	<16	<2	2
212	≥64	<16	128	<16	<2	2
145	<16	<16	≥512	<16	<2	4
234	<16	<16	≥512	<16	<2	4
235	≥64	<16	256	<16	<2	4
199	not tested		≥4096	32	<2	32

¹Pediatric sera (protocol 006)

²Historical titers

³Anti-human IgG used at 1:2 dilution

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MRK-CHA00026480

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Table 6
Enhancement of Mumps Neutralization with Anti-Human IgG

Serum #	Nt titer to Pre-serum at anti-IgG				Nt titer to Post-serum at anti-IgG			
	<u>1:4*</u>	<u>1:8*</u>	<u>Mock*</u>	<u>Historical</u>	<u>1:4</u>	<u>1:8</u>	<u>Mock</u>	<u>Historical</u>
98	<32	<32	<32	<2	≥4096	≥4096	<32	32
99	<32	<32	<32	<2	2048	2048	<32	8
101	<32	<32	<32	<2	2048	2048	128	128

* = dilution of anti-human IgG
 Nt titers with anti-IgG = using Low passage Jeryl Lynn™
 Historical titer = using Jeryl Lynn™ vaccine passage without anti-IgG treatment

DK 15 June 2000

Effect of Anti-Human IgG Treatment on **Mumps Antititers**

TABLE 5

sample #	anti human IgG dil	Pre serum	Post Serum
		NT titer	NT titer
238	undiluted	128	>=2048
238	1:2	128	>=2048
238	1:4	256	>=2048
238	1:8	256	>=2048
238	mock anti IgG	<32	32
321	undiluted	32	>=2048
321	1:2	<32	>=2048
321	1:4	<32	>=2048
321	1:8	<32	>=2048
321	mock anti IgG	<32	32
455	undiluted	32	>=2048
455	1:2	<32	>=2048
455	1:4	<32	>=2048
455	1:8	<32	>=2048
455	mock anti IgG	<32	32

Effect of Anti-Human IgG Treatment on **Mumps** **Titers**

DK, 8 June 2000

Table 7
Enhancement of Mumps Neutralization Using Anti-Human
 IgG

<u>Serum</u> ¹	<u>Nt titer to low-passage Jeryl Lynn™</u>				<u>Nt titer² to Jeryl Lynn™</u>	
	<u>Pre + anti-IgG³</u>	<u>Pre + PBS</u>	<u>Post + anti-IgG</u>	<u>Post + PBS</u>	<u>Pre</u>	<u>Post</u>
147	32	<16	≥512	<16	<2	<2
291	<16	<16	256	<16	<2	<2
4	≥64	<16	≥512	<16	<2	2
80	<16	<16	128	<16	<2	2
212	≥64	<16	128	<16	<2	2
145	<16	<16	≥512	<16	<2	4
234	<16	<16	≥512	<16	<2	4
235	≥64	<16	256	<16	<2	4
199	not tested		≥4096	32	<2	32

¹Pediatric sera (protocol 006)

²Historical titers

³Anti-human IgG used at 1:2 dilution

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 MRK-CHA00026483

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Mumps Plaque-Reduction Neutralization Assay Development Update
Backgrounder

June 20, 2000 CAS presentation

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MRK-CHA00026484**

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I. Executive Summary

A plaque-reduction neutralization assay using a low-passage Jeryl Lynn™ preparation is being optimized for use in evaluation of sera from the M-M-R@II Expiry Trial, with a goal of providing an assay that permits measurement of a $\geq 95\%$ seroconversion rate. The low-passage Jeryl Lynn™ virus has provided neutralization titers closest to those obtained using the vaccine-passage Jeryl Lynn™, and plaques are visualized by immunostaining. Optimization of the concentration of anti-human IgG for enhancement of the neutralization is underway. The utility of the Spearman-Kärber method to calculate titers is also being considered as a final refinement to maximize the capacity of the assay to detect seroconversions.

II. Background and status of assay development

A need for a mumps neutralization (Nt) assay utilizing a wild-type indicator virus has been identified to support analysis of the immune responses to mumps in the ongoing M-M-R@II Expiry Trial (Protocol 007). Efforts to date have focused on evaluating conditions that affect assay sensitivity and in defining a suitable indicator virus in a multi-well plate plaque-reduction neutralization assay (PRN).

A summary of the mumps strains and some of the virus growth and assay parameters evaluated is presented in Table 1. Previous studies comparing neutralization titers to sera from adult lab volunteers (who had either wild-type infections or mumps vaccine-induced responses) and pediatric sera showed an effect of the virus strain on neutralization titers, with the highest seroconversion rates and titers observed for the vaccine-passage of Jeryl Lynn™ mumps. CBER has indicated that the vaccine passage Jeryl Lynn™ is not suitable for use in the PRN and has established a requirement to use a “wild-type” mumps strain to evaluate vaccine-induced immune responses. A range of wild-type isolates were therefore obtained and evaluated in the PRN to identify the optimum indicator strain. In early testing, the Tennessee (TN) isolate provided Nt titers close to those obtained using Jeryl Lynn™, but further evaluation of this strain was aborted due to difficulties in reliably detecting plaques. Several plaque staining methods were evaluated, including Coomassie Blue (general cell stain) and neutral red or tetrazolium salts (vital stains), without consistent success.

In addition to “mechanical” aspects of the assay (incubation times and temperatures, virus attachment times), two supplements were evaluated for their capacity to increase the Nt sensitivity. Complement supplementation provided modest titer increases for adult sera and was complicated by the anti-mumps activity of the complement sera. Further evaluation of this reagent was therefore not pursued. A second supplement, anti-human Ig, was evaluated to confirm its ability to increase Nt titers (approximately 100-fold titer increases), but was not immediately pursued.

Subsequent studies shifted to use the London 1 strain (Lo1) of mumps, which was also used in studies performed at CBER. This strain met the criterion of being a “wild-type” virus and became the “virus of choice” for development of the PRN. Results of a series of pilot PRN assays of pediatric sera against Jeryl Lynn™, Lo1 and JL2 mumps strains showed respective seroconversion rates of

91% (63/69), 69% (43/62) and 56% (18/32). Testing of 169 paired sera from Protocol 006 (Competitive Trial) confirmed that the general assay format using Lo1 mumps would not provide the targeted $\geq 95\%$ seroconversion rate.

In parallel with the studies of Lo1 mumps, a sample of SBL-1 mumps (reportedly antigenically similar to Jeryl Lynn™) was obtained and evaluated in the PRN assay. SBL-1 mumps did not provide increased Nt performance versus Lo1 using a panel of pediatric and adult sera (Table 2).

Through discussion with CBER staff, the following suggestions and comments were made for evaluation in increasing the sensitivity of the PRN:

- The use of "Low-passage" JL (between passages 7 and 12) would be acceptable
- Consider assay format used by Dr. Bagher Forghani (The State of California Department of Health Services) that reportedly provides $>90\%$ seroconversion rates
 - Immunostaining (distinct "plaques" observed 3 days post-infection for all mumps strains tested in our hands).
 - Assay performed in 48-well plates
 - Evaluate the Barnes strain of mumps
- Consider using anti-human IgG to enhance Nt sensitivity
- Consider using the Spearman-Kärber method to calculate Nt titers

In response to these suggestions, stocks of the Barnes and low-passage Jeryl Lynn™ (lot 135 [passage 7], used at passage 8 in PRN assays) mumps viruses were obtained and evaluated in the PRN. Due to the low-cytolytic activity of these viruses, immunostaining (polyclonal goat anti-mumps antibody, peroxidase-labeled anti-goat IgG and peroxidase substrate) was adopted for detection of plaques. The immunostaining method was found to be universally applicable to detect mumps plaques (for all available strains), and therefore also permitted re-evaluation of previous strains such as TN. The 48- and 24-well plate formats (as alternatives to the 12-well plate format used in our previous studies) proved to be technically inconvenient for sample inoculation and were not pursued further.

A panel of adult lab volunteer sera was tested against Barnes, TN, Lo1, low-passage (lot 135, P8) Jeryl Lynn™ and vaccine passage Jeryl Lynn™ mumps indicator viruses to determine the relative Nt for the different viruses (Table 3). Nt titers to the low-passage lot 135 Jeryl Lynn™ mumps were comparable to those obtained using the vaccine-passage virus, and greater by 2-4-fold than those to Lo1, TN or Barnes mumps. TN and Lo1 titers were comparable and approximately 2-fold higher than those to the Barnes strain of mumps. Results of testing of a panel of 23 pediatric sera (selected to have a titer ≥ 128 from previous assays to permit further testing using small serum volumes) showed that Nt titers to the vaccine-passage virus were approximately 2-fold higher than those to the low-passage Jeryl Lynn™ and approximately 4-fold higher than those to Lo1 (Table 4). From the panel of wild-type mumps strains, the low-passage Jeryl Lynn™ virus therefore provides Nt sensitivity most close to the vaccine-passage virus.

The use of the Spearman-Kärber method to interpolate titers is expected to provide an increased number of seroconversions, but not to the targeted $\geq 95\%$

value. It is therefore expected that further enhancement of Nt by addition of anti-human IgG will be required. Previous studies demonstrated that this enhancement boosted post-vaccination titers approximately 100-fold, but the effect on pre-vaccination titers was not measured. In pilot studies, undiluted anti-human IgG provided positive titers to 75% of the pre-vaccination sera (9/12: titers ranging from 32 to 128) and 8-64-fold increases in post-vaccination titers, while lower amounts (1:2, 1:4 or 1:8 dilutions) of anti-IgG provided comparable enhancement of post-vaccination titers, but retained negative titers for 3/3 pre-vaccination sera (Table 5). The use of 1:4 or 1:8 dilutions of anti-IgG in a second study retained negative Nt responses for pre-vaccination sera (tested at an initial 1:32 dilution), and provided increases in titers for all three post-vaccination sera (Table 6). Results of a third experiment, using sera that previously provided titers of <2, 2 or 4, showed that a 1:2 dilution of anti-IgG permitted measurement of titer enhancements for all post-vaccination sera (Table 7). The amount of anti-IgG used in this study also resulted in positive Nt responses for several of the pre-vaccination sera. Current studies are focusing on determining the optimum concentration of anti-IgG to boost post-vaccination titers but not shift pre-vaccination sera to a positive Nt response.

III. Path forward

The proposed assay format will include:

- 12-well plate format
- Low-passage Jeryl Lynn™ indicator virus
- Enhancement of Nt with anti-human IgG
- Detection of plaques by immunostaining
- Calculation of Nt titers by 50% cutoff or Spearman-Kärber method

Current studies (4-5 weeks) are designed to determine the optimum amount of anti-IgG for Nt enhancement while retaining negative titers for pre-vaccination sera. An evaluation can then be made of the effect of using the “50% Nt” cutoff (highest tested dilution tested that provides $\geq 50\%$ Nt) versus the Spearman-Kärber titer interpolation to finalize the assay format. It is proposed that the optimized assay format will then be applied to the sera from Protocol 006 (4 weeks after finalization of the assay format) to provide an estimate of the seroconversion rates detected.

Issues remaining to be addressed include:

- Serum dilutions to be tested
 - the assay produces a “prozone” effect at dilutions approximately ≤ 32
 - post-vaccination titers are expected to be increased approximately 100-fold
- Impact if a significant proportion of pre-vaccination sera register as Nt positive
- Impact if testing of “pre-evaluation” panel provides <95% seroconversion
- Transfer of the optimized assay

Table 1
Factors evaluated for effects on Mumps Nt sensitivity

- Indicator virus
 - Jeryl Lynn™
 - Swiss isolates
 - NY
 - TN
 - SA
 - Jones
 - Enders
 - Lo1
 - JL2
 - JL5
 - SBL-1
 - Barnes
 - Select viruses passaged in CEF vs Vero (Lo1, TN, Enders, Jones)
- Incubation time and temperature of virus and serum
- Virus concentration
- Virus harvest fractions and clarification methods
- Cell substrate for virus stock growth
- Staining method for plaque visualization
(Coomassie Blue, neutral red, tetrazolium salts, immunostaining)
- Virus attachment time
- Enhancements to Nt
 - Complement (≤ 8 -fold enhancement)
 - anti-human IgG (~100-fold enhancement)

Table 2
Evaluation of PRN Titers Using Jeryl Lynn™, Lo1 and SBL-1 Mumps Strains

<u>Serum</u>	<u>Nt titer using</u>		
	<u>Jeryl Lynn™</u>	<u>Lo1</u>	<u>SBL-1</u>
1 pre	<8	<8	<8
1 post	16	<8	8
2 pre	<8	16	<8
2 post	16	8	<8
3 pre	not tested		
3 post	<8	<8	<8
4 pre	not tested		
4 post	8	8	<8
5 pre	not tested		
5 post	16	8	<8
6 pre	<8	<8	<8
6 post	16	32	<8
7 pre	<8	<8	<8
7 post	<8	<8	<8
8 pre	<8	<8	<8
8 post	16	16	<8
Adult control 1	≥128	32	16
Adult control 2	16	16	4
Adult control 3	1024	512	256

10/25/2019
Declaration of G. Reilly
EXHIBIT 121

Fechtenburg, Linda

From: Morsy, Manal A.
Sent: Sunday, October 10, 1999 1:25 PM
To: Ukwu, Dr. Henrietta; Chirgwin, Keith D.
Cc: Fechtenburg, Linda
Subject: Re: highlights
Importance: High

Enclosed please find highlights I drafted for MMRII and MMRV. I left a copy this morning Sunday 10/10 in both of your offices for comments back.

Please note in the MMRII section I have stressed the need for obtaining total particle to infective particle count for all viruses used in the Neut. assay since I believe this is a critical piece of information needed for establishing technical feasibility or limitation of the currently used PRN and CPE assays.

With regards to the MMRV, I have modified slightly over what Keith and I had discussed previously.

I have not included highlights on OGOS, rHA and Japan, three area I have great discomfort with still.

If neither of you have comments back on the highlights I will distribute these out first thing Monday morning (10/11/99)

Thanks for your patients with me through this painful - challenging and exciting all at the same time - learning process



09-89.doc

Manal



MEMO

TO: Henrietta Ukwu **DATE:** October 8, 1999

CC: D. Blois, B. Buckland, C.Chan, H. Cohen, E. Emini, P. Kniskern, D. Krah, B. Kuter, L. Kuykens, S. Lenz, J. Lewis, W. Long, D. Margolskee, C. Russo, J. Sadoff, A. Shaw, R. Singhvi, E. Slater, J. Staub, S. Thaler, B. Thompson, R. Zeldin

FROM: Manal Morsy

SUBJECT: Monthly Highlights for September 1999 (M-M-R@II and MMRV)

M-M-R@II

- **End-expiry:** The expiry trial has now enrolled ~50% of the subjects (Target 1500). The primary study hypothesis of a SCR $\geq 90\%$ against WT mumps virus is unlikely to be met and therefore this should be revised either in terms of addressing the hypothesis or addressing the technical limitations of the assays used to date.

The implications of the low neutralizing antibody seroconversion rate in terms of study design and sample size require discussion with CBER. The timing for this discussion is dependent on the timing of the results of the M-M-R@II to Priorix comparison (data will be available by last week of October to 1st week of November).

Mumps neutralizing antibody assay: The results of the mumps plaque reduction neutralization (PRN) and cytopathic effect (CPE) assays were reviewed at the CAS. With JL as the test isolate, the SCR is ~90%, and with L01 as the test isolate, the SCR is ~70-75%. Prior to discussing the unanticipated low SCR for mumps with CBER, the sera from the head-to-head trial with M-M-R@II and Priorix will be assayed to confirm that this low SCR is observed with both products. The current timeline for this analysis is 4-6 weeks. An alternative assay that may overcome some of the potential technical limitations has been discussed. Preliminary data using a high throughput QPA based Neut. Assay will be generated to determine if greater sensitivity can be attained (Time line 4Q99 – 1Q01).

The key information requested and elements of the discussion with CBER about the mumps neutralizing antibody assay include:

- 1) review of the arguments that the current WT neutralizing antibody assay may not capture all attributable protective efficacy;
- 2) argue against the use of WT virus in the Neut. assays since SCR against JL is reproducible and confirms label claims using the current Neut. assays;
- 3) review the total particle count to infective virus ratio for JL and the WT viruses (LO1, S. African and Swiss) used in the Neut. assay. If ratios of abortive to infective particle across the 4 viruses are not identical, and if abortive to infective particle ratio in the WT viruses is greater than that in the JL vaccine for which tissue culture growth conditions have been optimized, an argument against using WT viruses can be build supported by the technical

limitations of the PRN and CPE Neut. assays. Technically, both assays can not account for the percent of Neut. antibodies lost to abortive particle (unless the difference in ratios between total particle count and infective virus for each of the viruses is factored in).

4) review the extensive field experience in support of vaccine protective efficacy;

5) revision of the mumps expiry trial study hypotheses (if all viruses used in Neut. assays have similar total particle count to infective particles as found in JL, then we would review the mumps expiry trial study hypotheses and remove >90% SCR hypothesis; retain equivalence hypothesis with consideration of an increase in the equivalence margin to avoid an untenable increase in the sample size).

MMRV

- Filing strategy: The current strategy will be to accelerate MMRV licensure in the U.S. by pursuing a frozen product. The target date for submitting a frozen MMRV BLA is 3Q01. A refrigerated product will be licensed in the U.S. as a variation to the initial frozen quadrivalent. The current target date for submitting this sBLA is 3Q02. U.S launch dates approved at TPAC are: Frozen MMRV (3Q02) and 4°C MMRV (3Q03)
 - Preparation for End-of-Phase II meeting with CBER: CBER concurrence with the CDP and registration package will be obtained at this meeting.
- Studies proposed for Phase III:
- 1) Consistency lots : proposed FPI 1Q00.
 - 2) Concomitant use: proposed FPI 2Q00.
 - 3) Expanded safety: proposed FPI 2Q00.
- Outstanding issues requiring further discussion and closure with CBER include:
 - 1) Acceptable surrogate markers: for measles, mumps and rubella. The current serologic (EIA) assays lack an established correlation with protective efficacy and CBER has indicated that a functional antibody assay (e.g. WT Neut) will be required to establish equivalence. However, evidence of a correlation between the current assays and a WT Neut assay, or evidence of correlation with protective efficacy, would allow the current EIA-based assays to be used. This approach may be more feasible with measles and rubella than mumps. The proposed approach to surrogate markers for demonstrating equivalence between MMRV and M-M-R®II plus VARIVAX® will be finalized and confirmed with CBER
 - 2) Demonstration of equivalence: Approach to demonstrating equivalence with the licensed monovalent (VARIVAX®) and trivalent (MMR®II).
 - 3) Statistical criteria for success: The acceptable equivalence margins for each antigen.
 - 4) Expiry dose selection:(minimum acceptable immunogenicity). Preliminary data from the dose-ranging trial (25% accrual) was reviewed. These data will determine whether a feasible expiry dose (function of the maximum manufacturable release dose and estimated stability – 28,000 pfu PUVV is the release dose selected in the Consistency lot trial – protocol 013) provides adequate immunogenicity. Frozen MMRV must provide equivalent immunogenicity to the licensed monovalent.
 - 5) Consistency evaluation: (details of clinical consistency evaluation, lot selection) – protocol reviewed and approved at CDOC – Oct. 6
 - 6) Proposed product profile and label

Timing: An End-of-Phase II meeting is a Type B meeting under PDUFA, which means that the meeting should be scheduled to occur within 60 days of the FDA receiving the written

meeting request. The background document must be submitted no later than 30 days before the scheduled meeting date. Since the phase II dose-ranging data are an essential element of this background document, the timing for this CBER meeting is closely linked to the timing of availability of these data. At the present time the plan is to request a meeting for the 2-3 week in December.

MM
UN-B121

cc: file, chron

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10/25/2019
Declaration of G. Reilly
EXHIBIT 122

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA : CIVIL ACTION
ex rel., STEPHEN A. : NO. 2:10-04374 (CDJ)
KRAHLING and JOAN A. :
WLOCHOWSKI, :
Plaintiffs, :
vs. :
MERCK & CO., INC., :
Defendant. :

: Master File No.

IN RE: MERCK MUMPS : 2:12-cv-03555 (CDJ)
VACCINE ANTITRUST :
LITIGATION :

THIS DOCUMENT RELATES TO: :
ALL ACTIONS :

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July 11, 2017

Videotaped deposition of DAVID KRAH,
taken at the offices of Spector Roseman &
Kodroff, 1818 Market Street, Suite 2500,
Philadelphia, Pennsylvania 19103, beginning at
8:58 a.m., before LINDA ROSSI-RIOS, a
Federally Approved RPR, CCR and Notary Public.

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5 SPECTOR ROSEMAN & KODROFF, P.C.	5	
6 BY: JOHN A. MACORETTA, ESQUIRE	6 By Mr. Keller 10	
7 and	7	
8 DIANA J. ZINSER, ESQUIRE	8 E X H I B I T S	
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18 On behalf of the Relators	18 Krah-4 2000 Journal, 74	
19 CONSTANTINE CANNON LLP	19 490081 - 490591	
20 BY: GORDON SCHNELL, ESQUIRE	20 Krah-5 2001 Journal, 74	
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22 DANIEL VITELLI, ESQUIRE	22	
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<p style="text-align: right;">Page 6</p> <p>1 EXHIBITS (cont'd.)</p> <p>2 Krah-27 Handwritten note, 241 448146</p> <p>3</p> <p>4 Krah-28 2/24/99 E-mail with 253 attachments, 95046 - 95053</p> <p>5</p> <p>6 Krah-29 Series of e-mails, 271 51640 - 51642</p> <p>7 Krah-30 3/30/00 E-mail, 275 336323 - 336325</p> <p>8</p> <p>9 Krah-31 Subcommittee meeting 283 agenda, 2142149</p> <p>10</p> <p>11 Krah-32 Anti-IgG Enhanced Mumps 286 Neutralizing Assay-Update: October 24, 2000, 26912 - 26918</p> <p>12</p> <p>13 Krah-33 Series of e-mails with 311 attachment, 759836 - 759847</p> <p>14</p> <p>15 Krah-34 11/29/00 Memo, 330 1218 - 1221</p> <p>16</p> <p>17 Krah-35 Plaque Reduction 331 Neutralization Assay for Mumps Analytical Validation Protocol (v.01), 780112 - 780116</p> <p>18</p> <p>19 Krah-36 Series of e-mails, 338 52848 & 5284</p> <p>20</p> <p>21 Krah-37 Plaque Reduction 347 Neutralization Assay for Mumps Analytical Validation Protocol (v.02), 337307 - 337318</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 7</p> <p>1 EXHIBITS (cont'd.)</p> <p>2 Krah-38 12/10/99 E-mails, 363 52242</p> <p>3</p> <p>4 Krah-39 2/22/01 Fax, 383 780093 & 780094</p> <p>5</p> <p>6</p> <p>7</p> <p>8</p> <p>9</p> <p>10</p> <p>11</p> <p>12</p> <p>13</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 8</p> <p>1 DEPOSITION SUPPORT INDEX</p> <p>2</p> <p>3 DIRECTION TO WITNESS NOT TO ANSWER</p> <p>4 Page Line</p> <p>5 23 15</p> <p>6</p> <p>7</p> <p>8</p> <p>9 REQUEST FOR PRODUCTION OF DOCUMENTS</p> <p>10</p> <p>11 Page Line</p> <p>12 (None)</p> <p>13</p> <p>14</p> <p>15 STIPULATIONS</p> <p>16 Page Line</p> <p>17 (None)</p> <p>18</p> <p>19</p> <p>20</p> <p>21 QUESTIONS MARKED</p> <p>22</p> <p>23 Page Line</p> <p>24 (None)</p> <p>25</p>	<p style="text-align: right;">Page 9</p> <p>1 - - -</p> <p>2 VIDEOGRAPHER: We are now on the</p> <p>3 record. Please note the microphones</p> <p>4 are sensitive and may pick up</p> <p>5 whispering and private conversations.</p> <p>6 Turn off all cell phones and place them</p> <p>7 away from microphones. They can</p> <p>8 interfere with the deposition audio.</p> <p>9 My name is Dan Grbich</p> <p>10 representing Veritext.</p> <p>11 The date today is July 11, 2017,</p> <p>12 and the time is approximately 8:58 a.m.</p> <p>13 This deposition is being held at</p> <p>14 Spector Roseman & Kodroff, located at</p> <p>15 1818 Market Street, Philadelphia,</p> <p>16 Pennsylvania. The caption of this case</p> <p>17 is In Re: Merck's Mumps Vaccine</p> <p>18 Antitrust Litigation, United States of</p> <p>19 America, ex rel, Stephen A. Krahling</p> <p>20 and Joan Wlochowski versus Merck & Co.,</p> <p>21 Inc. This is being held in the United</p> <p>22 States District Court for the Eastern</p> <p>23 District of Pennsylvania. The name of</p> <p>24 the witness is David Krah.</p> <p>25 All attorneys will be marked</p>
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<p style="text-align: right;">Page 10</p> <p>1 present on the stenographic record. 2 At this time our court reporter, 3 Linda Rossi of Veritext will swear in 4 the witness and you may proceed. 5 - - - 6 DAVID KRAH, after having been 7 first duly sworn, was examined and 8 testified as follows: 9 - - - 10 EXAMINATION 11 - - - 12 BY MR. KELLER: 13 Q. Good morning, Dr. Krah. Can you 14 state your full name for the record? 15 A. Yes. David L. Krah. 16 Q. And how old are you? 17 A. 61. 18 Q. 61. What is your current 19 residence address? 20 A. 213 Brunswick Court, Lansdale, 21 PA. 22 Q. You've lived there for quite a 23 while? 24 A. Yeah, I think 28 or 29 years, I 25 believe.</p>	<p style="text-align: right;">Page 12</p> <p>1 has spent some time with you explaining the 2 rules and sort of what to expect today, but it 3 always helps for us to kind of do it again 4 just to kind of go over it to make sure that 5 we're all on the same page and you sort of 6 understand what's going to happen and so that 7 there's no confusion at the end of the day 8 when the case -- the transcript in this case 9 is written up. 10 As you can see, Linda is going 11 to take down everything we say. Though she's 12 amazing, it's very difficult for her to take 13 down when we speak at the same time. She will 14 be able to do it, but at the end of the day 15 when they -- I'm sure when you were deposed 16 before, you saw a thing called a transcript 17 which had all the questions and answers. So 18 we really want to have a complete question and 19 a complete answer, not have them jumbled 20 together, which is what happens when people 21 speak over each other. So for purposes of 22 today and tomorrow, please allow me to finish 23 my question and you will see -- you'll get the 24 hang of this pretty quickly, but you'll see 25 that sometimes it may take me a second to</p>
<p style="text-align: right;">Page 11</p> <p>1 Q. Have you ever had your deposition 2 taken before? 3 A. Yes. 4 Q. How many times? 5 A. Once. 6 Q. When was that? 7 A. The late '90s. 8 Q. Is that with regard to your work 9 or personal? 10 A. Work. 11 Q. Do you recall the nature of that 12 lawsuit? 13 A. Yes. 14 Q. What was the nature of that 15 lawsuit? 16 A. The nature was a claim, as best 17 I can recall, that Merck and Beacon were 18 making against GlaxoSmithKline for the 19 varicella vaccine. 20 Q. And let me come back to that in 21 a minute. 22 When you had your deposition 23 taken in that case in the 1990s, I'm sure they 24 went over the ground rules about how a 25 deposition takes place. I'm sure your counsel</p>	<p style="text-align: right;">Page 13</p> <p>1 formulate the second half of my question. Get 2 the first part down, then I have to figure out 3 the second part. Just give me a second to 4 finish my question and then I will do my best 5 to allow you to finish answering. Is that 6 fair? 7 A. Yes. 8 Q. Perfect. And you're doing a 9 great job with using words to answer. Though 10 the court reporter can probably pick up 11 uh-huhs and uh-uhs, for a clear record, we 12 want a clear record, yeses or noes and using 13 words instead of nonverbal communication. Is 14 that fair? 15 A. Yes. 16 Q. You were interviewed by the 17 Department of Justice. Do you recall that? 18 A. Yes. 19 Q. And how many days were you 20 interviewed for? 21 A. One. 22 Q. One day. You understand in that 23 interview you were under penalty of perjury 24 when you answered their questions. Correct? 25 MR. SANGIAMO: Objection. You</p>

4 (Pages 10 - 13)

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<p style="text-align: right;">Page 14</p> <p>1 can answer.</p> <p>2 THE WITNESS: I don't recall</p> <p>3 giving the oath as I did at the</p> <p>4 beginning of this. I don't know.</p> <p>5 BY MR. KELLER:</p> <p>6 Q. You don't know.</p> <p>7 Were you truthful when you spoke</p> <p>8 to the Department of Justice?</p> <p>9 A. Yes.</p> <p>10 Q. At the end of our two days here,</p> <p>11 Linda will prepare a transcript and you'll</p> <p>12 have a chance to review that transcript and</p> <p>13 make changes as you deem appropriate. Just be</p> <p>14 aware that any changes that you make we'll be</p> <p>15 able to make reference to that at trial.</p> <p>16 Okay? So if you change your testimony in the</p> <p>17 transcript, we will be able to use your</p> <p>18 prior -- the original testimony and your</p> <p>19 changes. Do you understand that?</p> <p>20 MR. SANGIAMO: Let me just</p> <p>21 interpose, Jeff, the rules are what</p> <p>22 they are. We'll proceed according to</p> <p>23 the rules.</p> <p>24 MR. KELLER: Fair enough, Dino.</p> <p>25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 16</p> <p>1 medical conditions that would affect your</p> <p>2 ability to tell the truth today? Just yes or</p> <p>3 no.</p> <p>4 A. No.</p> <p>5 Q. Who is representing you today?</p> <p>6 A. Pardon me?</p> <p>7 Q. Who is representing you today?</p> <p>8 Are these Merck's lawyers or your personal</p> <p>9 lawyers?</p> <p>10 MR. SANGIAMO: I'm serving as</p> <p>11 both Merck's counsel and Dr. Krah's</p> <p>12 counsel.</p> <p>13 BY MR. KELLER:</p> <p>14 Q. Is that true?</p> <p>15 A. Yes.</p> <p>16 Q. When did you -- let me back up</p> <p>17 to the 1990s when you had the case with</p> <p>18 varicella.</p> <p>19 Who sued who with regard to the</p> <p>20 varicella vaccine?</p> <p>21 A. I recall that Merck and Beacon</p> <p>22 were involved. I don't recall specifically</p> <p>23 who the actual entity was that was suing GSK,</p> <p>24 GlaxoSmithKline.</p> <p>25 Q. And GSK was trying to develop</p>
<p style="text-align: right;">Page 15</p> <p>1 Q. One of the most important rules</p> <p>2 here is if you do not understand my question,</p> <p>3 and you don't say anything, we're all going to</p> <p>4 assume that you did. So if I ask a question</p> <p>5 you don't understand, please let me know;</p> <p>6 otherwise, we're all going to assume that the</p> <p>7 answer you gave was -- that you understood the</p> <p>8 question. Is that fair?</p> <p>9 A. Yes.</p> <p>10 Q. We are entitled to your best</p> <p>11 understanding. We don't want you to guess at</p> <p>12 anything, but we are entitled to your best</p> <p>13 understanding. So if you need to -- you know,</p> <p>14 if you don't know specifically an answer but</p> <p>15 you know generally of an answer, you still</p> <p>16 need to answer, though you can identify that</p> <p>17 to the extent that you have your knowledge. I</p> <p>18 remember something, I don't remember</p> <p>19 everything. But you can't say I don't</p> <p>20 remember when you remember something. Is that</p> <p>21 fair?</p> <p>22 A. Yes.</p> <p>23 Q. Is there any reason today why</p> <p>24 you can't have your deposition taken? Are you</p> <p>25 on any sort of medication? Have you any</p>	<p style="text-align: right;">Page 17</p> <p>1 their own varicella vaccine?</p> <p>2 A. They were trying to develop a</p> <p>3 varicella vaccine, yes.</p> <p>4 Q. With a different virus strain?</p> <p>5 A. No.</p> <p>6 Q. Same virus strain?</p> <p>7 A. Yes.</p> <p>8 Q. Do you know -- do you recall</p> <p>9 whether or not -- where that case was venued?</p> <p>10 Was it in federal court or state court?</p> <p>11 A. I recall it was in Delaware, but</p> <p>12 I don't recall whether it was federal or</p> <p>13 state.</p> <p>14 Q. Why were you deposed in that</p> <p>15 matter?</p> <p>16 A. I had -- it was my understanding</p> <p>17 why I was deposed is that I had a detailed</p> <p>18 understanding of the varicella manufacturing</p> <p>19 process and had -- including information that</p> <p>20 we gained from Beacon.</p> <p>21 Q. Did Beacon, was that the entity</p> <p>22 that developed the varicella vaccine and did</p> <p>23 Merck purchase it from them?</p> <p>24 MR. SANGIAMO: Object to the</p> <p>25 form.</p>

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<p style="text-align: right;">Page 18</p> <p>1 BY MR. KELLER: 2 Q. Let me rephrase that. Who 3 developed the varicella vaccine that was at 4 issue in this lawsuit? 5 MR. SANGIAMO: Objection. You 6 can answer. 7 THE WITNESS: There are parts of 8 the process that were developed by 9 Beacon and then parts of the process 10 that were extended, from my understanding, 11 at the different, either Merck or GSK. 12 In this case it was GSK. 13 BY MR. KELLER: 14 Q. You stated earlier that you were 15 familiar with the manufacturing practice of 16 the varicella vaccine. How did you become 17 knowledgeable about that topic? 18 A. I didn't say practice. Process. 19 The process. 20 Q. Sorry, I misheard you. 21 A. I became familiar with that 22 through two -- two -- actually at least one is 23 interacting with our manufacturing group at 24 Merck to understand the manufacturing process 25 that Merck was using. Also I was requested to</p>	<p style="text-align: right;">Page 20</p> <p>1 along with me, but I was able to get 2 firsthand information about the 3 discussions with Beacon. 4 BY MR. KELLER: 5 Q. Was that in preparation to 6 take -- to sit for a deposition or was that 7 information you had before you were being 8 called as a witness? 9 MR. SANGIAMO: Objection. 10 THE WITNESS: That was 11 information that was before I was 12 deposed. 13 BY MR. KELLER: 14 Q. So that's information you had as 15 part of your normal job duties at Merck in 16 working on that particular vaccine? 17 A. Yes. 18 MR. SANGIAMO: Objection. 19 BY MR. KELLER: 20 Q. When did you first learn that 21 you were going to be deposed in this case? 22 A. I can't remember a specific 23 date. I would say sometime last year there 24 was a suggestion that I would be deposed. 25 Q. What did you do in -- did you do</p>
<p style="text-align: right;">Page 19</p> <p>1 and made a trip to the -- to Beacon. It's -- 2 when I refer to Beacon, it's -- I'm trying to 3 remember the name. It's -- Osaka University 4 is, I think, like the parent organization. 5 Beacon, as best I recall, is the manufacturing 6 part of that. So at any point I made a visit 7 to both Beacon and Osaka University, talked to 8 one of the people that began the development 9 of the vaccine to ask questions, understand 10 details about their manufacturing process. 11 Q. Were you -- I don't want you to 12 disclose any communications with counsel, but 13 do you know whether or not you were testifying 14 as a person most knowledgeable or based on 15 your -- let me -- let me just start with that. 16 Were you testifying as a person most 17 knowledgeable for the company? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: I wouldn't say I 21 was most knowledgeable. I would say 22 that it's my understanding that I -- 23 since I had direct experience 24 interacting with Beacon, that that 25 was -- there were others on the trip</p>	<p style="text-align: right;">Page 21</p> <p>1 anything to prepare for your deposition today 2 since last year when you first learned about 3 it? 4 MR. SANGIAMO: Object to the 5 form. 6 THE WITNESS: Can you clarify as 7 far as specific examples? 8 BY MR. KELLER: 9 Q. What did you do personally? Did 10 you do anything personally to help prepare 11 yourself for today's deposition? 12 A. I didn't do anything. The only 13 thing I did do was meet with counsel for the 14 preparation sessions. 15 Q. How many sessions did you have? 16 A. I believe five. 17 Q. And were those full-day sessions? 18 A. I believe. As best I can 19 recall, yes. 20 Q. And when was the first full-day 21 session? 22 A. I don't recall. 23 Q. When was the last time you met? 24 A. Yesterday. 25 Q. And did you meet for a full day</p>

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Page 22	<p>1 yesterday?</p> <p>2 A. It was the majority of the day.</p> <p>3 Q. And before yesterday, when did</p> <p>4 you meet before that?</p> <p>5 A. Friday, last Friday.</p> <p>6 Q. And that was, again, a full day?</p> <p>7 A. The majority of the day.</p> <p>8 Q. What about before that?</p> <p>9 A. I think -- as best I recall,</p> <p>10 Thursday of last week.</p> <p>11 Q. And before that?</p> <p>12 A. I don't recall.</p> <p>13 Q. So you met yesterday and two</p> <p>14 days last week. Correct?</p> <p>15 A. As best I can recall, yes.</p> <p>16 Q. And then the other two meetings,</p> <p>17 do you recall when those occurred?</p> <p>18 A. They were within the last few</p> <p>19 weeks, but I don't recall specific dates.</p> <p>20 Q. Prior to the last few weeks,</p> <p>21 have you spoken to Merck's counsel regarding</p> <p>22 this case?</p> <p>23 MR. SANGIAMO: That's a yes or</p> <p>24 no, Dave.</p> <p>25 THE WITNESS: Yes.</p>	Page 24	<p>1 several years ago?</p> <p>2 A. It was several years ago, but I</p> <p>3 don't recall the date.</p> <p>4 Q. Did you read the Amended</p> <p>5 Complaint?</p> <p>6 A. I recall seeing parts of it. I</p> <p>7 didn't read every part of it.</p> <p>8 Q. What part do you recall seeing?</p> <p>9 A. I don't recall.</p> <p>10 Q. Do you recall discussing the</p> <p>11 Complaint? Do you recall reviewing with</p> <p>12 anybody at Merck, excluding any attorneys?</p> <p>13 A. I did not discuss it with anyone</p> <p>14 else.</p> <p>15 Q. Have you -- so you did not</p> <p>16 discuss this case with anybody other than</p> <p>17 Merck's lawyers?</p> <p>18 A. That's correct.</p> <p>19 Q. Are you married?</p> <p>20 A. No.</p> <p>21 Q. Do you have a girlfriend?</p> <p>22 A. Not currently.</p> <p>23 Q. And during the time that you</p> <p>24 first learned about this lawsuit, did you have</p> <p>25 a girlfriend between then and now?</p>
Page 23	<p>1 BY MR. KELLER:</p> <p>2 Q. And how many conversations have</p> <p>3 you had?</p> <p>4 MR. SANGIAMO: I'm going to</p> <p>5 object to that.</p> <p>6 THE WITNESS: I don't recall.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. Was it more than one?</p> <p>9 A. It's more than one.</p> <p>10 Q. Was it less than ten?</p> <p>11 MR. SANGIAMO: That's invading</p> <p>12 the attorney-client privilege.</p> <p>13 MR. KELLER: The number of</p> <p>14 conversations?</p> <p>15 MR. SANGIAMO: Yeah. I'm going</p> <p>16 to instruct him not to answer that.</p> <p>17 BY MR. KELLER:</p> <p>18 Q. You're going to follow your</p> <p>19 counsel's instruction?</p> <p>20 A. Yes.</p> <p>21 Q. In preparation -- let me ask</p> <p>22 you, when did you first learn about this</p> <p>23 lawsuit?</p> <p>24 A. I don't recall a specific date.</p> <p>25 Q. Was it -- do you recall, was it</p>	Page 25	<p>1 A. Not that I recall.</p> <p>2 Q. In preparation for your</p> <p>3 deposition today, over those five full-day</p> <p>4 meetings that you had with your counsel, did</p> <p>5 you look at documents?</p> <p>6 A. Yes.</p> <p>7 Q. Do you recall how many documents</p> <p>8 you looked at?</p> <p>9 A. That, I don't recall.</p> <p>10 Q. More than one?</p> <p>11 A. Yes.</p> <p>12 Q. Less than 100?</p> <p>13 A. I can't say with any --</p> <p>14 Q. Can you give me your best</p> <p>15 recollection of how many documents?</p> <p>16 A. There were at least -- they're</p> <p>17 running together in my head, so I can't really</p> <p>18 give a...</p> <p>19 Q. It could have been two or it</p> <p>20 could have been 500?</p> <p>21 A. I can't recall the specific</p> <p>22 number. It's more than two, I would say. I</p> <p>23 don't recall.</p> <p>24 Q. So it could have been three?</p> <p>25 Sir, I'm trying to get fair testimony from</p>

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<p style="text-align: right;">Page 26</p> <p>1 you. If you -- how big of a stack of 2 documents can you recall looking at? 3 MR. SANGIAMO: You know, Jeff, 4 the documents that are reviewed in 5 preparation for a deposition are work 6 product. So you're certainly not 7 allowed to ask him what those documents 8 were. I'd have to think about whether 9 you're allowed to ask him how many he 10 looked at, but I don't see where that's 11 going since you're not going to be able 12 to ask him what he looked at. He's 13 given you his best recollection. 14 BY MR. KELLER: 15 Q. Sir, did you look at a Bankers 16 Box worth of documents? 17 A. I can't -- there were -- as best 18 I can recall, there were documents one at a 19 time, and I -- there was no pile or assembly 20 that would remind me of how many there were. 21 Q. Can you recall how many 22 documents you looked at in an hour? 23 MR. SANGIAMO: Objection. 24 THE WITNESS: Some documents -- 25 all I can offer for that is that some</p>	<p style="text-align: right;">Page 28</p> <p>1 A. Yes. 2 Q. How many journals did you 3 maintain? Let me rephrase that question. 4 The journal that you maintained, 5 was that kept on a computer program? 6 A. Yes. 7 Q. What was the -- did that 8 computer program change over the years? 9 A. As best I can recall, it was 10 Microsoft Word. I don't recall how that 11 changed over time. 12 Q. And did you keep more than one 13 journal? 14 A. There -- the -- I'll say yes in 15 that there was one general format for the 16 journal but over multiple years, and they were 17 saved as separate -- by different years. So 18 they exist as separate documents but are -- 19 one could view them as a continuation. 20 Q. So other than segregating them 21 out by year in separate files, did you keep 22 any separate personal journals? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: Not --</p>
<p style="text-align: right;">Page 27</p> <p>1 documents took -- were reviewed more 2 quickly than others. So I can't 3 exclude that some took an hour to 4 review and others were less than an 5 hour. 6 BY MR. KELLER: 7 Q. I'm asking how many documents do 8 you recall looking at in an hour on average? 9 A. That, I don't recall. 10 Q. You can't tell. Okay. How many 11 documents did you look at yesterday? 12 A. That, I don't recall. 13 Q. Have you looked at any 14 deposition transcripts in this case? Did you 15 review any deposition transcripts in this 16 case? 17 A. For this case? 18 Q. Yes. 19 A. No. 20 Q. Did you look at any deposition 21 summaries in this case? 22 A. No. 23 Q. Sir, over the course of your 24 professional life at Merck, did you maintain a 25 journal?</p>	<p style="text-align: right;">Page 29</p> <p>1 BY MR. KELLER: 2 Q. Let me rephrase the question. 3 Did you keep a journal at home? 4 A. No. 5 Q. Did you maintain any documents 6 at home from Merck? 7 A. No. 8 Q. Do you have a personal computer 9 at home? 10 A. I have my work computer. 11 Q. That's a laptop? 12 A. Currently it's a laptop, yes. 13 Q. And back in -- let me just sort 14 of back up. 15 Back in the late '90s, did you 16 have a laptop? 17 A. I don't recall -- I don't recall 18 when the Merck laptop was issued. I don't 19 recall in the late '90s if we had a laptop 20 or -- I didn't have a personal laptop. 21 Q. Did you have a personal computer 22 at home? 23 MR. SANGIAMO: In the late '90s? 24 MR. KELLER: Yes. 25 THE WITNESS: Not that I recall.</p>

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1 BY MR. KELLER:
 2 Q. Did you have a desktop computer?
 3 A. At work?
 4 Q. At home.
 5 A. At home, no.
 6 Q. Do you have a personal computer
 7 at home currently?
 8 A. No.
 9 Q. During -- so from the late '90s
 10 to today you've never had a personal computer
 11 at home?
 12 A. Not that I recall.
 13 Q. Back to your journals that you
 14 maintained on Word, did you ever have separate
 15 journals for work stuff and another journal
 16 for personal stuff?
 17 A. I did not have a separate
 18 journal, but I did, on occasion, excerpt
 19 information from the one journal into a
 20 separate compilation, but it was the same
 21 information that was in the primary journal.
 22 Q. So your journal kept all the
 23 information that you -- let me strike that.
 24 When I say "strike," it means I'm just going
 25 to do it over again and forget that question.

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1 So did you ever delete
 2 information from your journal?
 3 A. Not that I recall other than a
 4 typographical error.
 5 Q. But you would copy things from
 6 your journal and move them into a different
 7 file for other purposes. Correct?
 8 A. There are occasions where that
 9 was done.
 10 Q. And under what occasions would
 11 that occur, if you can recall, between the
 12 late '90s and current?
 13 A. If there was a -- one example
 14 perhaps is if we had -- if there was a topic
 15 where I wanted to compile information over the
 16 course of time into one document so that it
 17 was all that topic rather than sorting through
 18 the original journal, then I would do that
 19 compilation.
 20 Q. So for personnel issues you
 21 would compile information about somebody's --
 22 if they were late multiple times, you would
 23 copy that out of your journal into a
 24 compilation?
 25 MR. SANGIAMO: Object to the

Page 32

1 form. You can answer.
 2 THE WITNESS: Not -- I think
 3 that specific example I do not recall
 4 doing.
 5 BY MR. KELLER:
 6 Q. What specific example do you
 7 recall?
 8 A. If there were personnel issues
 9 or personnel discussions that I thought
 10 were -- that were continuing that I wanted to
 11 compile, I would excerpt the information from
 12 the journal into a separate summary on that
 13 personnel topic.
 14 Q. Well, in the case of a personnel
 15 issue, why would you be excerpting different
 16 references from different days into a
 17 compilation?
 18 A. One application for that would
 19 be to compile, if there was a trend of
 20 behavior or trend of events. And then include
 21 efforts I was making to try to understand or
 22 address the questions.
 23 Q. What did you do with that
 24 information once you compiled it?
 25 MR. SANGIAMO: Object to the

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1 form. You can answer.
 2 THE WITNESS: For the most part,
 3 as best I can recall, I would just have
 4 it available for reminding me of the
 5 summaries. I can't exclude that on
 6 some cases that was forwarded to
 7 management for review.
 8 BY MR. KELLER:
 9 Q. Did you ever recommend that
 10 somebody get fired from your lab?
 11 A. Yes.
 12 Q. How many times did that happen?
 13 A. Twice.
 14 Q. And do you recall when that
 15 happened?
 16 A. I don't recall the dates, but I
 17 remember the occasions.
 18 Q. Can you describe those occasions?
 19 A. One was -- they were both
 20 contract employees in the lab. One was
 21 someone who had come to us, as best I can
 22 recall, in her resume claiming extensive lab
 23 experience on a particular topic. When she
 24 came to the lab, she showed none of those
 25 skills and, in fact, was missing many

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<p style="text-align: right;">Page 34</p> <p>1 rudimentary skills. I had her work with 2 multiple people in the lab throughout the 3 course of a week to see if everyone would have 4 the same observation. They confirmed that 5 this person wasn't -- appeared that they had 6 basic lab skills. We recommended to the 7 contract agency that she be terminated. 8 Q. The second occasion? 9 A. The second occasion was another 10 contract employee who, as best I can recall, 11 was, I would say, technically competent but 12 not -- from my recollection, not very 13 interested -- not interested in the work that 14 he was doing, was not completing assignments 15 on time. And after several weeks, we 16 recommended that he be terminated. 17 Q. Did you ever recommend any Merck 18 employees be terminated? 19 A. No. 20 Q. Did you ever recommend any Merck 21 employees be demoted? 22 A. No. 23 Q. Let me ask you, in response to 24 this litigation, did you do anything to search 25 for any of your -- any documents that you kept</p>	<p style="text-align: right;">Page 36</p> <p>1 Q. Do you currently have your own 2 office? 3 A. I have an office where there's 4 no other person in the office. 5 Q. Do you maintain files in your 6 office? 7 A. Yes. 8 Q. Did you ever go through those 9 files to see if there's any documents that are 10 related to this lawsuit? 11 A. Yes. 12 Q. Did you provide those documents 13 to your counsel? 14 A. Yes. 15 Q. Did anybody else search those 16 files other than you? 17 MR. SANGIAMO: Answer if you 18 know. 19 THE WITNESS: A group came to 20 retrieve the files. I don't know if 21 that counts as counsel or not. But I 22 don't recall who they were. 23 BY MR. KELLER: 24 Q. So just so I understand, the 25 procedure that you followed in order to</p>
<p style="text-align: right;">Page 35</p> <p>1 in your files? 2 A. No. 3 Q. And your -- when did you start 4 Merck? 5 A. 1988. 6 Q. And since 1988, have you ever 7 brought any documents home from work? 8 A. Yes. 9 Q. And what kind of documents did 10 you bring home? 11 A. I believe, as best I can recall, 12 minutes of meeting or -- meeting minutes or 13 agendas. 14 Q. Why did you bring those home? 15 A. To review, or if I didn't have 16 time to review them at work, to be able to 17 review them before the next day or whatever 18 the -- whatever I needed to review them. 19 Q. Was that an acceptable policy at 20 Merck? 21 MR. SANGIAMO: Objection. 22 Answer if you know. 23 BY MR. KELLER: 24 Q. To your understanding. 25 A. To my understanding, yes.</p>	<p style="text-align: right;">Page 37</p> <p>1 produce documents in this case from the files 2 that you maintained in your office is that you 3 went through those files, segregated them and 4 then somebody came by and picked them up? 5 MR. SANGIAMO: Object to the 6 form. 7 Dr. Krah, you should not 8 disclose the content of communications 9 with counsel on this topic. 10 BY MR. KELLER: 11 Q. You can answer, though. Do you 12 need the question back? 13 A. There was no -- I did not 14 segregate any documents. 15 Q. So you just opened your office 16 files to somebody to come look or did you -- 17 strike that. 18 You testified a minute ago that 19 you went through your files and provided them 20 to somebody to come pick up. Did somebody 21 go -- did you provide them all of your files 22 or a subset of the files? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: I provided all the</p>

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<p style="text-align: right;">Page 38</p> <p>1 files that were -- that had any 2 relationship to the litigation. 3 BY MR. KELLER: 4 Q. And you made that decision 5 yourself? 6 A. Yes. 7 Q. And so -- did that include files 8 outside of your physical office? 9 MR. SANGIAMO: Object to the 10 form. 11 BY MR. KELLER: 12 Q. Do you understand my question? 13 A. I don't. 14 Q. Yes or no? 15 A. No, I don't understand. 16 Q. If you don't understand it, just 17 say I don't understand. That's fine. That 18 wasn't a great question, I'll try to rephrase 19 it. 20 Did you also look for documents 21 responsive, that related to this case outside 22 of the files that are kept in your physical 23 office? 24 MR. SANGIAMO: Object to the 25 form.</p>	<p style="text-align: right;">Page 40</p> <p>1 form. 2 THE WITNESS: Can you clarify as 3 far as what are -- 4 BY MR. KELLER: 5 Q. How do you maintain your files 6 in your lab? Let me back up and get some more 7 foundation here. 8 The lab that you currently work 9 in, how long have you been in that lab? 10 A. Perhaps 14 years. 11 Q. 14 years. So around 2003, where 12 did you -- did you work in a different lab? 13 A. Yes. 14 Q. Where -- from 2003 to today, 15 what's the -- does the lab have a location 16 identifier? 17 A. Yes, there are room numbers. 18 Q. And what was the room number for 19 the lab that you've worked in since 2003 to 20 current? 21 A. There's -- if I maybe qualify 22 this in that there's the lab, there's an 23 office area by the lab, so the labs themselves 24 are 309 and -- building 16, room 309 and 327. 25 Q. And then there's an office that</p>
<p style="text-align: right;">Page 39</p> <p>1 THE WITNESS: There were 2 documents that were kept in our 3 laboratory, and those were provided. 4 BY MR. KELLER: 5 Q. Did you do the same -- go 6 through the same procedure of going through 7 those files that were in your lab identifying 8 those that you believe related to the case and 9 then provided those to counsel? 10 MR. SANGIAMO: Object to the 11 form. 12 THE WITNESS: As best I recall, 13 I provided an index of the experiments 14 and provided those to counsel, and 15 counsel determined which files were 16 relevant. 17 BY MR. KELLER: 18 Q. So you only provided an index of 19 the experiments. Did you provide an index of 20 all the different documents that you had? You 21 had more than just -- more than -- strike 22 that. 23 Is there a centralized filing 24 system that you have in your lab? 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 41</p> <p>1 you maintain near that lab. Correct? 2 A. Yes. 3 Q. That's from 2003 to current. 4 Correct? 5 A. Yes, as best I recall. 6 Q. Now, from the time before 2003, 7 before you worked -- had a lab in room 309 and 8 327, you worked in a different lab. Correct? 9 A. We had two other labs -- two 10 other labs, we were using those, the 309 and 11 327 labs periodically but not exclusively. 12 Q. What other lab did you work in 13 more often? 14 A. The other labs were same 15 building 16, room 203, 213 and periodically 16 212. 17 Q. And so did you maintain the same 18 office -- they're in the same building. 19 Correct? 20 A. Yes. 21 Q. And those labs are organized -- 22 did you maintain the same office during that 23 time frame? 24 A. I moved my office, I believe, 25 twice during that time.</p>

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1 Q. In the same building?
 2 A. In the same building.
 3 Q. On the same floor?
 4 A. No.
 5 Q. So that when you -- they're on
 6 different floors. Prior to 2003 you were on
 7 the second floor, after 2003 you moved to the
 8 third floor. Correct?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: The labs that we
 12 were using were on the third floor 2003
 13 and beyond. So the labs that we
 14 were -- primary labs that we were using
 15 were on the second floor approximately
 16 2003 and then third floor after 2003.
 17 BY MR. KELLER:
 18 Q. So you moved your offices in
 19 2003 from the second floor to the third floor?
 20 MR. SANGIAMO: Object to the
 21 form.
 22 THE WITNESS: If I could clarify.
 23 What I was referring to were the
 24 laboratories. Laboratories in my view
 25 are separate from the offices.

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1 BY MR. KELLER:
 2 Q. Is it fair to say that the
 3 office, there's offices on each floor.
 4 Correct?
 5 MR. SANGIAMO: Object to the
 6 form.
 7 THE WITNESS: Not all the time.
 8 BY MR. KELLER:
 9 Q. On the second and third floor of
 10 building 16, there's offices on each floor?
 11 MR. SANGIAMO: Object to the
 12 form.
 13 BY MR. KELLER:
 14 Q. Let me just sort of cut through
 15 this if you can. Can you describe, when you
 16 were working -- when you had labs on the
 17 second floor, 203 and 213 and sometimes 212,
 18 how long were you in those labs? Just to get
 19 some more foundation.
 20 A. I was using those labs since I
 21 started in 1988.
 22 Q. 1988, okay. Why did you move to
 23 the third floor?
 24 A. As best I recall, the second
 25 floor was being renovated.

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1 Q. As part of your move in 2003,
 2 did you move your office?
 3 A. My office did move, but I don't
 4 recall that it was part of that renovation
 5 move or not.
 6 Q. When the office moved, did it
 7 move from the second floor to the third floor?
 8 A. My office did not --
 9 MR. SANGIAMO: Object to the
 10 form.
 11 BY MR. KELLER:
 12 Q. Your office stayed on the second
 13 floor?
 14 A. No.
 15 Q. Where did it move to?
 16 A. The first floor.
 17 Q. The first floor, okay. And
 18 so -- and that was in 2003, do you recall?
 19 A. I don't recall the date of that.
 20 Q. When you moved your offices, you
 21 don't recall the date, did you -- did somebody
 22 come in and move all your file cabinets? Let
 23 me back up a second.
 24 How did you keep your documents
 25 prior to 2003, your files that you maintain in

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1 your office?
 2 MR. SANGIAMO: Object to the
 3 form.
 4 THE WITNESS: Can you clarify
 5 what you mean by how I kept them?
 6 BY MR. KELLER:
 7 Q. Did you have files in your
 8 office?
 9 A. Yes.
 10 Q. Were they kept in file cabinets?
 11 A. Yes.
 12 Q. Were they kept anywhere else?
 13 A. There were some experiments that
 14 were kept on shelves.
 15 Q. And so what experiments would
 16 you keep on shelves?
 17 A. They were experiments that were
 18 in notebook binders that were -- lab
 19 experiments that were in binders.
 20 Q. And those binders, are those
 21 called workbooks?
 22 A. No. They're like -- I view them
 23 as like three-ring binders. Like, I don't
 24 know, there must be other names for them. I
 25 wouldn't call them a workbook.

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<p style="text-align: right;">Page 46</p> <p>1 Q. So those were your experimental 2 -- experiments that you were running, you kept 3 those in binders in your office? 4 MR. SANGIAMO: Object to the 5 form. 6 THE WITNESS: Not all experiments 7 were kept in binders, but I did have 8 experiments in binders. 9 BY MR. KELLER: 10 Q. What did you keep in your file 11 cabinets? 12 MR. SANGIAMO: Object to the 13 form. You can answer. 14 BY MR. KELLER: 15 Q. In this 2003 through -- 1998 16 through 2003 period. 17 A. A variety of documents and some 18 of the lab experiments. 19 Q. When you moved your offices, did 20 somebody come in and move all the binders on 21 the shelves and all the file cabinets? 22 A. Someone did move them. I packed 23 them up and somebody moved them. 24 Q. When you packed them up, did you 25 go through them and discard anything?</p>	<p style="text-align: right;">Page 48</p> <p>1 moved back to the, what was the 2 previous office on the first floor. 3 BY MR. KELLER: 4 Q. So these moves were -- you moved 5 to a temporary office when they were 6 renovating and you moved back to your original 7 office? 8 A. There were two renovations 9 involved. So one move was related to 10 renovation of the second floor, I don't recall 11 that they're exactly the same time, but then 12 when I moved to the first floor, there was a 13 renovation that was happening there as well 14 and I had to move to a temporary spot. 15 Q. So the files that were 16 maintained in the labs in 203, 213 and 212, 17 when you moved to the labs at 309 and 327, did 18 those file cabinets -- did those files get 19 moved as well? 20 A. Some of the documents from it 21 were moved to my office and some were moved -- 22 and I don't recall what percentage of them 23 were moved to the new file cabinets in the 24 third floor space. 25 Q. Were any documents destroyed, do</p>
<p style="text-align: right;">Page 47</p> <p>1 A. No. 2 Q. So those documents that were in 3 your office from 1998 through 2003, those were 4 moved when you moved your offices. Correct? 5 MR. SANGIAMO: Object to the 6 form. 7 THE WITNESS: All of the 8 documents that I had at the time of the 9 move were moved. 10 BY MR. KELLER: 11 Q. You said you moved again twice. 12 And the same, did you go through the documents 13 when you moved the next time to see -- to sort 14 through and get rid of anything or did you 15 just move everything to the next office? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: I can't exclude 19 that in the next move that I didn't 20 sort through -- I think examples are 21 like old journal articles that I didn't 22 feel were relevant anymore. But as 23 best I can recall, all other documents 24 were moved wholesale into the, I'll say 25 a temporary office and then eventually</p>	<p style="text-align: right;">Page 49</p> <p>1 you recall? 2 A. No. 3 Q. When you -- in response to this 4 case when you were looking -- when you were 5 going through the documents to identify 6 documents that were relevant to this case, you 7 also searched the files in the labs in rooms 8 309 and 327 in building 16. Correct? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: There were -- as 12 best I recall, there were no files in 13 those laboratories. 14 BY MR. KELLER: 15 Q. So the only files that you 16 recall searching that were relevant were in 17 your office. Correct? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: That's not fully 21 correct. The third floor, not in the 22 laboratory space, we had an office 23 space, a shared office space by the 24 laboratories, and there were files 25 there.</p>

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1 BY MR. KELLER:
 2 Q. You searched those files?
 3 A. Yes.
 4 Q. You determined what was relevant
 5 and you gave those to your lawyers. Correct?
 6 A. In that case --
 7 MR. SANGIAMO: Object to the
 8 form. You can answer.
 9 THE WITNESS: In that case, at
 10 least as best I can recall, we provided
 11 the indexes of the lab experiments to
 12 counsel and counsel reviewed them and
 13 decided what was relevant.
 14 BY MR. KELLER:
 15 Q. Was there anything other than
 16 lab experiments in those file cabinets?
 17 A. Not that I recall.
 18 Q. Were there -- did you maintain
 19 any notes that were not in lab experiments as
 20 part of the ordinary course of running your
 21 labs? In the files that you maintained in
 22 your office after 2003, or in a shared office,
 23 were those just experiments?
 24 A. I'm sorry, the first half of
 25 that, did you say in my office were the only

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1 experiments?
 2 Q. Let me ask -- I'll break it up.
 3 In your office, did you maintain just lab
 4 experiments?
 5 A. No.
 6 Q. What else did you maintain?
 7 A. Reports, minutes of meetings,
 8 journal articles, safety information, manuals,
 9 equipment manuals.
 10 Q. And so you went through those to
 11 determine what was relevant to provide your
 12 counsel?
 13 MR. SANGIAMO: Object to the
 14 form.
 15 THE WITNESS: I reviewed it to
 16 identify what was relevant to provide
 17 them.
 18 BY MR. KELLER:
 19 Q. Did anybody else review them
 20 other than you?
 21 A. Not that I recall.
 22 Q. Did you -- you said that you
 23 would bring documents home periodically as
 24 part of the ordinary course of your job at
 25 Merck to review. Did you ever keep those

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1 documents at your house in a file?
 2 A. No.
 3 MR. SANGIAMO: Object to the
 4 preamble of your question. If you want
 5 to ask what they were kept in, that's
 6 fine.
 7 THE WITNESS: I never retained
 8 anything. They were returned to Merck.
 9 - - -
 10 (Exhibits Krah-1, Curriculum
 11 vitae, 00000695 - 00000702, was marked
 12 for identification.)
 13 - - -
 14 BY MR. KELLER:
 15 Q. Let me mark as Exhibit 1 a
 16 document that bears Bates stamp number 695
 17 through 702, which is an older CV of yours,
 18 sir. Can you tell me if you recognize this
 19 document?
 20 A. I can't say that I recall the
 21 specific date on it, but the general content
 22 looks familiar to me.
 23 Q. When is the last time you saw
 24 this document?
 25 A. The one dated January 1998?

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1 Q. Yes.
 2 A. That, I don't recall.
 3 Q. Do you have a current CV?
 4 A. Yes.
 5 Q. Did you provide that to counsel?
 6 A. I don't recall.
 7 Q. Can you take a second and tell
 8 me if there's anything in this CV that you
 9 believe to be -- is this -- to be accurate as
 10 of the date of January 1998?
 11 MR. SANGIAMO: I'm sorry, what
 12 was your question, Jeff?
 13 BY MR. KELLER:
 14 Q. Can you take a look at this and
 15 tell me if you think it to be correct as of
 16 January 1998? Let me strike that.
 17 Did you prepare this CV?
 18 A. I don't recall if I prepared it
 19 or one of our administrative associates
 20 prepared it.
 21 Q. Do you have any reason to
 22 believe that the information in here is
 23 incorrect?
 24 MR. SANGIAMO: Take your time
 25 and look through it if you need to.

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<p style="text-align: right;">Page 54</p> <p>1 MR. KELLER: In fairness I will 2 identify for the record that page 7 of 3 this CV is missing from the production 4 that was given to us. 5 THE WITNESS: I don't have any 6 reason to expect that anything is not 7 correct. 8 BY MR. KELLER: 9 Q. So the education and employment 10 history, that's accurate. Correct? 11 A. To the best of my understanding, 12 yes. 13 Q. So after 1998 -- I'm sorry, 14 after 1995, it says you are the "Senior 15 Research Fellow Department of Virus and Cell 16 Biology." Do you see that? Can you tell me 17 what your positions were from 1998 through 18 current? I don't have a current CV, so we 19 have to fill in the gap. So if you can 20 identify what your employment history is at 21 Merck after 1995 to fill in the gaps in the 22 CV. 23 A. The title names have changed 24 over the years. As best I can recall, 1998 I 25 was promoted to senior investigator.</p>	<p style="text-align: right;">Page 56</p> <p>1 principal scientist or something of that sort. 2 Q. It's the same level? 3 A. Yes. 4 Q. So from 1998 to 2017 you've had 5 the same job? 6 A. Yes. 7 Q. What is -- so if I say senior 8 investigator, is that a fair way to describe 9 your title? How would you like me to describe 10 your title between 1998 and 2017? 11 A. Senior investigator is as good 12 as any. It's just a set of words. 13 Q. Fair enough. And did your job 14 duties change from 1998 to 2017? 15 A. So projects changed. I don't 16 know if one could infer from that 17 responsibilities changed. There's a broad -- 18 so there's not a -- it's my understanding a 19 formal change of -- range of job 20 responsibilities between 1998 and present. 21 Q. Sorry, I didn't mean to 22 interrupt you. 23 MR. SANGIAMO: Are you done with 24 your answer? 25 THE WITNESS: I guess getting to</p>
<p style="text-align: right;">Page 55</p> <p>1 Q. That is the department of virus 2 and cell biology? 3 A. Our department name changed many 4 times so I think that -- like we were virus 5 and cell biology and cellular/microbiology and 6 then -- I can't -- I don't recall how many -- 7 it's in the same theme of virus and cell 8 biology. The department number changed and 9 the name changed, but the same entity, 10 basically. The same group. It was still in 11 the same group. 12 Q. The same management group? 13 A. Yes. 14 Q. Your job duties were the same 15 even though the department may have changed 16 names? 17 A. Within a given -- within a given 18 job title, yes. 19 Q. So in 1998 you were promoted to 20 a senior investigator. Correct? 21 A. The best I can recall is 1998. 22 Q. Can you tell me your next 23 promotion or next position? 24 A. That's been -- still the same 25 level. Now, the name has changed to senior</p>	<p style="text-align: right;">Page 57</p> <p>1 the point that the -- there are core 2 job responsibilities for a given 3 position, but the project 4 responsibilities can vary between 5 projects even with the same title. 6 BY MR. KELLER: 7 Q. You're researching different -- 8 you may be researching different viruses. 9 Correct? 10 A. Yes, as an example. 11 Q. Can you just give me a 12 description of what you do as a senior 13 investigator during this time frame? I 14 understand you worked on different projects, 15 but is there a way to describe what your job 16 responsibilities were in a very general way? 17 MR. SANGIAMO: You said this 18 time frame, that being? 19 BY MR. KELLER: 20 Q. 1998 to 2017 you've had the same 21 job title, and my question is, were you 22 generally doing the same work? 23 A. There were some -- I would break 24 it up into two time periods. 25 Q. Sure.</p>

15 (Pages 54 - 57)

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1 A. From 1998 through 2013 I was in
 2 some version of virus and cell biology.
 3 Again, I don't recall the name of the
 4 department at the time. With the
 5 responsibility of, as best I can recall,
 6 applying cell biology and virology to answer
 7 questions for projects that the project --
 8 that the department was supporting. That
 9 ranged from looking at alternate cell
 10 substrates for virus growth, increasing
 11 productivity, evaluating different virus
 12 strains, looking into animal models for
 13 infection. So a range of applications. My
 14 responsibility was to lead a group who
 15 contributed to that area.
 16 Q. These are basically research
 17 projects. Correct?
 18 A. Yes.
 19 Q. So you were a research lab.
 20 Correct?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: We were a lab in a
 24 research department.
 25 BY MR. KELLER:

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1 Q. Did you do any manufacturing
 2 testing?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 MR. KELLER: Strike that.
 6 BY MR. KELLER:
 7 Q. Did you work with Merck
 8 manufacturing on any of the products that were
 9 on the market for purposes of -- let me strike
 10 that.
 11 So you said that you were doing
 12 research under virus and cell biology. Those
 13 projects were changed based on whatever the
 14 department was interested in pursuing.
 15 Correct? Is that fair?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: Our -- the
 19 department had objectives, the research
 20 labs had objectives, and our department
 21 had objectives that were a subset of
 22 that. And then our lab contributed to
 23 whatever the objectives were for the
 24 area.
 25 BY MR. KELLER:

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1 Q. What do you mean by -- can you
 2 describe what you mean by an objective?
 3 A. Objective meaning work on a
 4 specific program or in our case largely
 5 vaccines. In my personal experience, largely
 6 vaccines.
 7 Q. Do you consider yourself to be
 8 an expert in vaccine research?
 9 A. I consider myself --
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: -- to be an expert
 13 in cell biology and virology. Perhaps
 14 less so in the cell biology, more so in
 15 the virology part. Not specifically in
 16 vaccine research.
 17 BY MR. KELLER:
 18 Q. And so -- and that's your
 19 educational training, is in virology. Correct?
 20 A. Yes.
 21 Q. Can you tell me during this time
 22 frame -- let me sort of narrow this down a
 23 little bit.
 24 Between 1998 and 2002, how many
 25 people were in your lab that you had

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1 responsibility for?
 2 A. I don't recall specific number.
 3 I would estimate between four and something
 4 more than four. I don't remember the upper
 5 number.
 6 Q. Were there people that reported
 7 to you that other people reported to in your
 8 lab --
 9 MR. SANGIAMO: Object to the
 10 form.
 11 BY MR. KELLER:
 12 Q. -- during this time frame 1998
 13 to 2002?
 14 A. There -- as far as formal
 15 reporting structure, everyone reported to me.
 16 There were some informal, I don't know if they
 17 called it reporting structure, but someone who
 18 might oversee other -- another group's
 19 activities in the lab.
 20 Q. During this time frame, from
 21 1988 to 2002, I'm going to talk about that for
 22 a while. Unless I say otherwise, that's the
 23 time frame I'm talking about for purposes of
 24 this series of questions. This informal
 25 reporting structure, who was -- was there a

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Page 62	<p>1 second in command in your lab at this time</p> <p>2 frame?</p> <p>3 MR. SANGIAMO: Object to the</p> <p>4 form.</p> <p>5 THE WITNESS: There were</p> <p>6 people -- or there were people, some</p> <p>7 people with more seniority than others.</p> <p>8 I wouldn't characterize them as second</p> <p>9 in command.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Ever hear that term used at</p> <p>12 Merck before?</p> <p>13 A. I've heard it used in general</p> <p>14 before. I don't -- can't say that</p> <p>15 specifically specific to Merck or that I heard</p> <p>16 it at Merck.</p> <p>17 Q. So in terms of the more</p> <p>18 seniority, who had the highest seniority in</p> <p>19 your lab during this time frame?</p> <p>20 A. Mary Yagodich.</p> <p>21 Q. Did you depend on Ms. Yagodich --</p> <p>22 MR. SANGIAMO: Object.</p> <p>23 BY MR. KELLER:</p> <p>24 Q. -- to oversee certain aspects of</p> <p>25 the lab?</p>	Page 64	<p>1 form.</p> <p>2 THE WITNESS: There is one other</p> <p>3 person who -- I don't know if it fits</p> <p>4 into the seniority part, but another</p> <p>5 person, DeeMarie Watson who --and this</p> <p>6 actually may precede 1998, the dates.</p> <p>7 Had her oversee largely a group of</p> <p>8 contract employees while another group</p> <p>9 of the lab was busy with other</p> <p>10 activities.</p> <p>11 BY MR. KELLER:</p> <p>12 Q. So Ms. Yagodich, she's a</p> <p>13 virologist as well?</p> <p>14 MR. SANGIAMO: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: Her undergraduate</p> <p>17 education, I -- actually, I don't</p> <p>18 recall what her undergraduate degree is</p> <p>19 in. Her undergraduate education would</p> <p>20 not be focused on virology, but from</p> <p>21 her experience in the lab, I would</p> <p>22 consider her a virologist.</p> <p>23 BY MR. KELLER:</p> <p>24 Q. You believe her to be competent?</p> <p>25 A. Yes.</p>
Page 63	<p>1 MR. SANGIAMO: Object to the</p> <p>2 form. You can answer.</p> <p>3 THE WITNESS: I looked to Mary</p> <p>4 to be the most highly trained,</p> <p>5 experienced person in the lab who I</p> <p>6 would go to to ask questions or have</p> <p>7 her -- if other people needed help,</p> <p>8 help her go to them.</p> <p>9 As far as -- I forget what your</p> <p>10 original --</p> <p>11 BY MR. KELLER:</p> <p>12 Q. I'm trying to get this formal --</p> <p>13 MR. SANGIAMO: I'm sorry, what</p> <p>14 is it?</p> <p>15 BY MR. KELLER:</p> <p>16 Q. Let me just -- we just stepped</p> <p>17 on each other. Let me ask the question again</p> <p>18 if you're done answering. Are you done</p> <p>19 answering?</p> <p>20 A. Yes.</p> <p>21 Q. Other than Mary Yagodich, was</p> <p>22 there anybody else in this informal hierarchy</p> <p>23 that you thought of as having seniority in</p> <p>24 terms of overseeing other people?</p> <p>25 MR. SANGIAMO: Object to the</p>	Page 65	<p>1 Q. Honest?</p> <p>2 A. Yes.</p> <p>3 Q. Do you recall that she had a</p> <p>4 good memory?</p> <p>5 MR. SANGIAMO: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: I recall that she</p> <p>8 was fluid in the work she that was</p> <p>9 doing. Whether that constitutes a good</p> <p>10 memory, I can't say.</p> <p>11 BY MR. KELLER:</p> <p>12 Q. Do you recall her -- let me back</p> <p>13 up.</p> <p>14 Did you have a romantic</p> <p>15 relationship with her?</p> <p>16 A. No.</p> <p>17 Q. Were you in love with her?</p> <p>18 A. No.</p> <p>19 Q. Did you ever date anybody's</p> <p>20 family members in the lab?</p> <p>21 A. Yes.</p> <p>22 Q. And who was that?</p> <p>23 A. Sister of Mary Yagodich.</p> <p>24 Q. So you were close to Mary?</p> <p>25 MR. SANGIAMO: Object to the</p>

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Page 66	<p>1 form.</p> <p>2 THE WITNESS: Not -- I was close</p> <p>3 to her being a long time member of the</p> <p>4 laboratory, not because of any other</p> <p>5 factor.</p> <p>6 BY MR. KELLER:</p> <p>7 Q. Did you ever socialize with her</p> <p>8 outside the office?</p> <p>9 A. I remember one occasion, at a</p> <p>10 Christmas party when she first moved into her</p> <p>11 house. That's the only event I recall.</p> <p>12 Q. Did you ever socialize with</p> <p>13 anybody in the lab outside of the office?</p> <p>14 A. Periodically the group would go</p> <p>15 to a restaurant or bar like Friday's after</p> <p>16 work. I remember going once, so not on a -- I</p> <p>17 do recall doing it occasionally, but not on a</p> <p>18 regular basis.</p> <p>19 Q. Did you ever take any of your</p> <p>20 employees to lunch? Let me strike that.</p> <p>21 Did you ever take anybody in</p> <p>22 your lab that you had supervisory</p> <p>23 responsibilities over to lunch?</p> <p>24 A. I did take lab members to</p> <p>25 Christmas lunches. There were other lunches</p>	Page 68	<p>1 '95. Do you see that?</p> <p>2 A. Yes.</p> <p>3 Q. Was that required to take GMP</p> <p>4 training yearly at Merck --</p> <p>5 MR. SANGIAMO: Object to the</p> <p>6 form.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. -- through this 1998 through</p> <p>9 2002 period? Let me back up.</p> <p>10 Did you take GMP -- let me</p> <p>11 strike that.</p> <p>12 What does GMP -- what's your</p> <p>13 understanding of GMP?</p> <p>14 A. It's a changing target of</p> <p>15 technically CGMP, current good manufacturing</p> <p>16 practices, reflecting whatever the</p> <p>17 expectations are or requirements at the time</p> <p>18 for manufacturing things like clinical</p> <p>19 supplies or indoor manufactured product or</p> <p>20 product for human use.</p> <p>21 Q. Do you know what the difference</p> <p>22 between CGMP is and Good Clinical Practices?</p> <p>23 A. No.</p> <p>24 Q. You never were trained in that?</p> <p>25 A. I don't recall being trained in</p>
Page 67	<p>1 that I attended, I don't know if that qualifies</p> <p>2 as taking them. I was with them at lunch.</p> <p>3 Q. Would that include the entire</p> <p>4 lab or just a subset of the lab --</p> <p>5 MR. SANGIAMO: Object to the</p> <p>6 form.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. -- during this time frame 1998</p> <p>9 to 2002?</p> <p>10 MR. SANGIAMO: Same objection.</p> <p>11 THE WITNESS: I recall at least</p> <p>12 on one occasion it was a subset of the</p> <p>13 lab. The majority of the cases were</p> <p>14 the full lab or whoever was either</p> <p>15 interested or available to come.</p> <p>16 BY MR. KELLER:</p> <p>17 Q. If you turn back to Exhibit 1,</p> <p>18 under "TRAINING," it appears that there's --</p> <p>19 in the first reference it says, "Good</p> <p>20 Manufacturing Practices for Biologics and</p> <p>21 Vaccines" in 1989.</p> <p>22 Do you see that?</p> <p>23 A. Yes.</p> <p>24 Q. And then you've got below that</p> <p>25 starting in 1992, "GMP Training," '93, '94,</p>	Page 69	<p>1 Good Clinical Practices.</p> <p>2 Q. Your lab was not certified as a</p> <p>3 GCP lab. Correct?</p> <p>4 MR. SANGIAMO: Object to the</p> <p>5 form.</p> <p>6 BY MR. KELLER:</p> <p>7 Q. At any time during the 1998 to</p> <p>8 2002 period?</p> <p>9 A. That, I can't say with</p> <p>10 certainty. I know we were inspected by Merck</p> <p>11 quality assurance, but I don't recall what</p> <p>12 the -- we passed the certification, but I</p> <p>13 don't recall what that certification included.</p> <p>14 Q. Was your lab GMP compliant?</p> <p>15 MR. SANGIAMO: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: As far as I can</p> <p>18 recall, we were not evaluated for --</p> <p>19 there was a period of time where we</p> <p>20 were evaluated in the early '90s in</p> <p>21 the -- from the 1998 to 2002 period, we</p> <p>22 weren't operating as a GMP laboratory,</p> <p>23 to the best of my understanding.</p> <p>24 BY MR. KELLER:</p> <p>25 Q. So you weren't operating as a</p>

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1 GMP lab from 1998 to 2002. Is that correct?
 2 A. I cannot exclude that there was
 3 a -- again, with the inspection that our
 4 internal quality assurance group did, what
 5 that -- what the outcome of that was, if that
 6 said that we were behaving as GMP or not. I
 7 don't recall.
 8 Q. You weren't trained in GMP
 9 compliance to run your lab. Correct?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: I did receive GMP
 13 training. As far as what GMP training
 14 would be needed to run the lab, I can't
 15 say that I know that there is specific
 16 training for that.
 17 BY MR. KELLER:
 18 Q. Was your lab ever certified as a
 19 GMP lab during this 1998 through 2002 time
 20 frame?
 21 A. Come back to the inspection that
 22 our quality assurance group did. We passed --
 23 I don't recall if that constitutes a
 24 certification.
 25 Q. That was just one inspection.

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1 Correct?
 2 A. Yes, that's the only one I
 3 recall.
 4 Q. And that came, that inspection
 5 occurred after the FDA inspected your lab.
 6 Correct?
 7 A. Yes.
 8 Q. And other than that one
 9 inspection, you don't recall ever being
 10 inspected by the CGMP folks at Merck?
 11 MR. SANGIAMO: Object to the
 12 form.
 13 THE WITNESS: Not during the
 14 1998 to 2002 period.
 15 BY MR. KELLER:
 16 Q. What about after?
 17 A. There was a -- we were doing
 18 some work, and this actually may fall into the
 19 2002 period, where we were working on an
 20 emergency vaccine program where our CGMP group
 21 did a review of our lab just to assess whether
 22 we were -- could make material under
 23 conditions appropriate for using it as an
 24 emergency vaccine.
 25 Q. Do you recall when that was?

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1 A. My first thought was it was
 2 after 2002, but it may have been -- it may
 3 have been in the late 2001 to 2002 period. I
 4 don't recall the date.
 5 Q. So there may have been another
 6 inspection with respect to that?
 7 A. Internal inspection by Merck to
 8 see if we would -- if our lab would be capable
 9 of making, basically, clinical supplies.
 10 Q. Do you recall the results of
 11 that inspection?
 12 A. I have a general recollection.
 13 They had recommendations and we complied with.
 14 I don't recall that they had major
 15 reservations.
 16 Q. Did you have any procedures in
 17 place to ensure compliance with GMP
 18 requirements?
 19 MR. SANGIAMO: Object to the
 20 form.
 21 THE WITNESS: We had SOPs, as
 22 best I can recall, that we obtained
 23 from the manufacturing division that we
 24 were using as a guide. Then we
 25 generated additional documents,

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1 additional SOPs within our department
 2 to try to be compliant with the GMP
 3 expectations.
 4 BY MR. KELLER:
 5 Q. That was after the FDA
 6 inspection in August of 2001. Correct?
 7 A. Yes.
 8 Q. But before that, you didn't have
 9 any SOPs?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: There were --
 13 documents existed, but I don't recall
 14 that we had any that were applying to
 15 the work that we were doing.
 16 MR. SANGIAMO: Jeff, we've been
 17 going about -- probably about an hour
 18 and ten, so when you get to a good
 19 stopping point.
 20 MR. KELLER: Take a break,
 21 that's fine.
 22 VIDEOGRAPHER: The time is now
 23 10:07. Going off the video record.
 24 - - -
 25 (A recess was taken.)

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<p style="text-align: right;">Page 74</p> <p>1 - - -</p> <p>2 VIDEOGRAPHER: The time is now</p> <p>3 10:26. This begins disc two. You may</p> <p>4 proceed.</p> <p>5 BY MR. KELLER:</p> <p>6 Q. Sir, I'm going to show you what</p> <p>7 has been -- we're going to mark as Exhibits 2</p> <p>8 through 19 which have been produced to us as</p> <p>9 your journals from 1999 through 2015. You</p> <p>10 testified earlier that you kept a journal in</p> <p>11 Microsoft Word. Correct?</p> <p>12 A. Yes.</p> <p>13 - - -</p> <p>14 (Exhibits Krah-2, 1998 Journal,</p> <p>15 488056 - 488404, Krah-3, 1999 Journal,</p> <p>16 455405 - 488932, Krah-4, 2000 Journal,</p> <p>17 490081 - 490591, Krah-5, 2001 Journal,</p> <p>18 490592 - 491038, Krah-6, 2002 Journal,</p> <p>19 491039 - 491419, Krah-7, 2003 Journal,</p> <p>20 491420 - 491835, Krah-8, 2004 Journal,</p> <p>21 489194 - 489500, Krah-9, 2005 Journal,</p> <p>22 488933 - 489193, Krah-10, 2006 Journal,</p> <p>23 489501 - 4897111, Krah-11, 2007</p> <p>24 Journal, 489903 - 490080, Krah-12, 2008</p> <p>25 Journal, 489712 - 489902, Krah-13, 2009</p>	<p style="text-align: right;">Page 76</p> <p>1 format?</p> <p>2 A. I recognize the format, yes.</p> <p>3 Q. Do you have any reason to</p> <p>4 believe that this is not a printout of your</p> <p>5 journal that you maintained in Microsoft Word?</p> <p>6 A. Yeah, I can't -- just to look to</p> <p>7 see if -- can't immediately verify</p> <p>8 completeness that there's not a day missing or</p> <p>9 something. But it looks like the format that</p> <p>10 I would use. And the dates look like they're</p> <p>11 covering the period that you mentioned.</p> <p>12 Q. Do you have any reason to</p> <p>13 believe that this is not a full and complete</p> <p>14 set of the journals that you maintained?</p> <p>15 MR. SANGIAMO: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: I have no reason</p> <p>18 to suspect or -- anticipate or expect</p> <p>19 that this is not a complete version.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. And the journal that you created</p> <p>22 from at least 1998 through 2015 that was</p> <p>23 produced to us, those journals were created in</p> <p>24 the ordinary course of your job duties at</p> <p>25 Merck. Correct?</p>
<p style="text-align: right;">Page 75</p> <p>1 Journal, 491836 - 492024, Krah-14, 2010</p> <p>2 Journal, 492025 - 492278, Krah-15, 2011</p> <p>3 Journal, 492279 - 492511, Krah-16, 2012</p> <p>4 Journal, 492516 - 4925738, Krah-17,</p> <p>5 2013 Journal, 486274 - 486490, Krah-18,</p> <p>6 2014 Journal, 486593 - 486830, Krah-19,</p> <p>7 2015 Journal, 486491 - 486592, were</p> <p>8 marked for identification.)</p> <p>9 - - -</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Let me show you Exhibit 2 which</p> <p>12 I put in front you, sorry, which is the 1998</p> <p>13 journal. Take a look at Exhibit 2, starts at</p> <p>14 Bates stamp number 488056, and tell me if you</p> <p>15 recognize this document as a journal from</p> <p>16 starting in 1998 through -- from January</p> <p>17 through the end of December for 1998?</p> <p>18 MR. SANGIAMO: Object to the</p> <p>19 form.</p> <p>20 THE WITNESS: Just to clarify,</p> <p>21 you're asking if this looks like one of</p> <p>22 my -- a journal that I had that spanned</p> <p>23 those periods that you mentioned?</p> <p>24 BY MR. KELLER:</p> <p>25 Q. Yes. Do you recognize the</p>	<p style="text-align: right;">Page 77</p> <p>1 MR. SANGIAMO: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: Are -- sorry.</p> <p>4 Just to clarify, are you asking if</p> <p>5 having a journal was part of my job</p> <p>6 duties or --</p> <p>7 BY MR. KELLER:</p> <p>8 Q. Yes, was it part of your job</p> <p>9 duties?</p> <p>10 A. It's not -- at least my</p> <p>11 understanding, it's not a requirement for my</p> <p>12 job.</p> <p>13 Q. Did you do it as part of your --</p> <p>14 though it wasn't a requirement, was it</p> <p>15 something that you did to help you perform</p> <p>16 your job at Merck?</p> <p>17 A. I did it to help increase my</p> <p>18 efficiency, for example, be able to recall</p> <p>19 or -- recall old information.</p> <p>20 Q. So you -- as part of your job</p> <p>21 duties, you used these journals that we've</p> <p>22 marked Exhibit 2 through 19 from 1998 through</p> <p>23 2015 as part of your -- to help you do your</p> <p>24 job at Merck. Correct?</p> <p>25 MR. SANGIAMO: Object to the</p>

20 (Pages 74 - 77)

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<p style="text-align: right;">Page 78</p> <p>1 form.</p> <p>2 THE WITNESS: I did it to help</p> <p>3 me be more efficient in my job at</p> <p>4 Merck.</p> <p>5 BY MR. KELLER:</p> <p>6 Q. Did anybody know -- did your</p> <p>7 superiors know that you were using a journal</p> <p>8 at Merck?</p> <p>9 MR. SANGIAMO: Object to the</p> <p>10 form.</p> <p>11 THE WITNESS: I can't say that</p> <p>12 they did or didn't, no.</p> <p>13 BY MR. KELLER:</p> <p>14 Q. Was it your practice during your</p> <p>15 time that you worked at Merck, at least from</p> <p>16 1998, you maintained a daily journal of</p> <p>17 your -- what you were -- strike that.</p> <p>18 What was the purpose of you</p> <p>19 maintaining a journal on a daily basis?</p> <p>20 A. The original intent, as best I</p> <p>21 can recall, is to keep track of experiments,</p> <p>22 both progress and experiments, in some cases</p> <p>23 experiment numbers, in some cases results of</p> <p>24 those experiments. And then additionally over</p> <p>25 time began to include summaries of meetings or</p>	<p style="text-align: right;">Page 80</p> <p>1 A. There are occasions where that</p> <p>2 was included.</p> <p>3 Q. Why would you capture a</p> <p>4 communication between another -- for example,</p> <p>5 a superior?</p> <p>6 MR. SANGIAMO: Object to the</p> <p>7 form.</p> <p>8 MR. KELLER: Let me strike that.</p> <p>9 BY MR. KELLER:</p> <p>10 Q. Did you ever capture communications</p> <p>11 with your superiors?</p> <p>12 A. Yes.</p> <p>13 Q. Who were your superiors, who did</p> <p>14 you report to from this 1998 to 2002 time</p> <p>15 frame?</p> <p>16 A. Alan Shaw.</p> <p>17 Q. Who did Alan Shaw report to?</p> <p>18 A. Emilio Emini.</p> <p>19 Q. Who did Mr. Emini report to?</p> <p>20 A. That, I don't recall.</p> <p>21 Q. During this time frame, did you</p> <p>22 ever have any communications with Emilio Emini?</p> <p>23 A. Yes.</p> <p>24 Q. Did you ever capture those in</p> <p>25 your journals?</p>
<p style="text-align: right;">Page 79</p> <p>1 points that I thought were relevant to being a</p> <p>2 more easily retrievable form for my personal</p> <p>3 efficiency.</p> <p>4 Q. You didn't use this journal for</p> <p>5 your personal life. Correct?</p> <p>6 A. I can't exclude that there were</p> <p>7 no -- in fact, I expect there are entries,</p> <p>8 have a car service done today or something</p> <p>9 like that. So it was a journal to keep track</p> <p>10 primarily of work-related things, but there</p> <p>11 are some work -- life-related events that I</p> <p>12 would have -- like reminders, for example.</p> <p>13 Q. Did it act as your calendar as</p> <p>14 well?</p> <p>15 A. It was a reminder for certain</p> <p>16 items that would be part of a calendar.</p> <p>17 Q. I noticed in your journals that</p> <p>18 some things had checks on it and some things</p> <p>19 just had bullet points.</p> <p>20 A. Yes.</p> <p>21 Q. What do the checks mean?</p> <p>22 A. The check typically means that</p> <p>23 that comment was completed or addressed.</p> <p>24 Q. And did you also capture</p> <p>25 communications with other Merck employees?</p>	<p style="text-align: right;">Page 81</p> <p>1 A. As best I can recall, yes.</p> <p>2 Q. Did you have any communications</p> <p>3 with Alan Shaw?</p> <p>4 A. Yes.</p> <p>5 Q. Did you capture those in your</p> <p>6 journals?</p> <p>7 MR. SANGIAMO: Object to the</p> <p>8 form.</p> <p>9 THE WITNESS: Yes.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Did you have communications with</p> <p>12 individuals in the lab that you captured in</p> <p>13 the journals during this 1998 to 2002 time</p> <p>14 frame?</p> <p>15 A. I don't recall specific examples,</p> <p>16 but I would anticipate so.</p> <p>17 Q. Do you have any reason to believe</p> <p>18 that the entries that you entered into your</p> <p>19 journals were inaccurate?</p> <p>20 MR. SANGIAMO: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: The entries that I</p> <p>23 made are, to the best of my understanding,</p> <p>24 my impression or -- so as far as whether</p> <p>25 they're accurate, I would say they</p>

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Page 82	<p>1 reflect my impression, my understanding.</p> <p>2 Whether that constitutes accuracy I</p> <p>3 guess one could debate, but there</p> <p>4 were -- it was -- represented my</p> <p>5 understanding.</p> <p>6 BY MR. KELLER:</p> <p>7 Q. And you would enter things in</p> <p>8 the journal contemporaneous when those things</p> <p>9 were happening. Correct?</p> <p>10 MR. SANGIAMO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: The objectives was</p> <p>13 to enter them as -- or ideally on the</p> <p>14 same day, but I can't guarantee that in</p> <p>15 all cases it was done on the same day.</p> <p>16 BY MR. KELLER:</p> <p>17 Q. Was part of the use of the</p> <p>18 journal to track the flow of the running of</p> <p>19 the experiments?</p> <p>20 A. In the context of -- so I'll say</p> <p>21 yes in the context of, for example, I recall</p> <p>22 cases where I would have a list of experiments</p> <p>23 that were in progress and then as they were</p> <p>24 completed, confirmation that they were</p> <p>25 completed so we can basically have a reminder</p>	Page 84	<p>1 as part of your duties as you described in</p> <p>2 your testimony?</p> <p>3 MR. SANGIAMO: Object to the</p> <p>4 form.</p> <p>5 THE WITNESS: The 2001, at least</p> <p>6 the format looks consistent with the</p> <p>7 format that I had used previously.</p> <p>8 There is -- this may have been an error</p> <p>9 in the date entry. The back end of it,</p> <p>10 the dates, the year kind of jumps from</p> <p>11 2001 back to 2000.</p> <p>12 BY MR. KELLER:</p> <p>13 Q. Did you understand that the</p> <p>14 journal, the Word -- the Microsoft Word --</p> <p>15 were there -- strike that.</p> <p>16 As part of you using Microsoft</p> <p>17 Word to do your daily journal entry, did you</p> <p>18 ever edit an entry?</p> <p>19 MR. SANGIAMO: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: Edit in what? Can</p> <p>22 you give an example?</p> <p>23 BY MR. KELLER:</p> <p>24 Q. Did you ever copy sections from</p> <p>25 one day and move it to the next day?</p>
Page 83	<p>1 of what is still to be completed.</p> <p>2 Q. Did you ever capture results in</p> <p>3 your journal of certain experiments?</p> <p>4 A. Yes.</p> <p>5 Q. Did you ever discuss issues</p> <p>6 within the lab in your journals, for example,</p> <p>7 problems with equipment?</p> <p>8 MR. SANGIAMO: Object to the</p> <p>9 form.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. During this 1998 to 2002 time</p> <p>12 period?</p> <p>13 MR. SANGIAMO: Same objection.</p> <p>14 THE WITNESS: I don't recall. I</p> <p>15 don't recall examples of that.</p> <p>16 BY MR. KELLER:</p> <p>17 Q. Let me do this: Let me give</p> <p>18 you -- take a look at Exhibit 4 and Exhibit 5</p> <p>19 which are the 2000 and 2002 journals and tell</p> <p>20 me if you -- I'm sorry, 2000 and 2000 --</p> <p>21 strike that.</p> <p>22 Let me show you Exhibits 4 and</p> <p>23 Exhibit 5 which are the 2000 and 2001</p> <p>24 journals. Can you tell me if you recognize</p> <p>25 those journals as journals that you prepared</p>	Page 85	<p>1 A. Yes.</p> <p>2 Q. Do you understand what metadata</p> <p>3 is? Metadata?</p> <p>4 A. I've heard the term before, but</p> <p>5 I can't say that I know what it means.</p> <p>6 Q. So you don't know whether or not</p> <p>7 the information that's at the back of these</p> <p>8 journals were captured in Microsoft Word and</p> <p>9 when the lawyers produced these documents,</p> <p>10 produced all the data that was in Microsoft</p> <p>11 Word but not viewable as your daily journal?</p> <p>12 MR. SANGIAMO: Object to the</p> <p>13 form.</p> <p>14 THE WITNESS: That's not a</p> <p>15 situation I'm aware of. The dates that</p> <p>16 I had questioned looked like the right</p> <p>17 dates. For example, on page 478, it's</p> <p>18 1/14/01, 1/15/01, 1/16/01, 1/17/01,</p> <p>19 1/18/01, 1/19/01, and then goes to</p> <p>20 1/21/00. So I -- I just point out it's</p> <p>21 a date discrepancy, but that it could</p> <p>22 have just as easily be that when I was</p> <p>23 putting the dates in, I entered for the</p> <p>24 balance from 1/22 -- I'm sorry,</p> <p>25 1/21/2001 on I put in 2000 as the year</p>

22 (Pages 82 - 85)

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1 instead of 2001.
2 BY MR. KELLER:
3 Q. Or you could have been -- do you
4 recall ever using the same file folder for
5 your journal and then moving that data into
6 the next year in a different file or do you
7 recall just every January 1st starting a new
8 file?
9 A. I at least -- the best of my
10 recollection, the practice I was using
11 typically was to, for the next year, include
12 -- this one that comes to mind, one going back
13 to December 1st of the previous year and carry
14 that over to the next year. So it wasn't a
15 January 1st to January 31st -- January 1st to
16 December 31st.
17 Q. That explains why the beginning
18 of every journal may have dates from December
19 the prior year?
20 A. Yes. Yes.
21 Q. Fair enough. Let me have you
22 look on the -- you're looking in the 2000
23 journal. Right?
24 A. Yes.
25 Q. Can you turn to page 428 of that

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1 journal? There's a page number at the top of
2 the journal.
3 A. Okay.
4 Q. Do you see that?
5 A. Okay. Yes.
6 Q. And here you have Wednesday,
7 December 6, 2000. Correct? Do you see that?
8 A. Yes.
9 Q. What is the first entry there?
10 A. What it says is "Start mumps
11 AIGENT assays for Protocol 007."
12 Q. Is that when you started running
13 the sera for Protocol 007?
14 A. I can't tell from this if that's
15 what that means.
16 Q. You understand what Protocol 007
17 is?
18 A. Yes, I'm familiar with it.
19 Q. What was Protocol 007?
20 A. My understanding of Protocol 007
21 was a study to compare the immunogenicity of
22 the mumps component of MMR at three different
23 doses.
24 Q. Was there any -- when you say --
25 is that -- do you understand what an objective

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1 is of a protocol?
2 MR. SANGIAMO: Object to the
3 form.
4 BY MR. KELLER:
5 Q. Let me back up.
6 Do you know what a protocol is?
7 A. I've heard of them and seen
8 them, but I can't say that I understand all
9 the components that are in there.
10 Q. And so did you ever see the
11 protocol for Protocol 007?
12 MR. SANGIAMO: Object to the
13 form.
14 THE WITNESS: I don't recall
15 seeing the full protocol. I can't
16 exclude that I saw some part of the
17 protocol.
18 BY MR. KELLER:
19 Q. What does the protocol, based on
20 your understanding, describe? What is the
21 purpose -- strike that.
22 What is the purpose of a
23 protocol?
24 A. It's an area outside of my
25 expertise. I've read them, I've seen them,

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1 but I can't speak with confidence about what
2 their -- the purpose is or what it includes.
3 Q. When you said that your
4 understanding of the Protocol 007 was to
5 compare the immunogenicity between three
6 doses, is that a fair statement of what you
7 just testified to?
8 A. That's my recollection of my
9 understanding.
10 Q. Did you understand that to be
11 the objective of Protocol 007?
12 MR. SANGIAMO: Object to the
13 form.
14 THE WITNESS: I can't say that
15 that is -- I don't know what the
16 objective -- the formal objective was.
17 That was in a practical way my
18 interpretation of what I thought the
19 purpose of the study was for.
20 BY MR. KELLER:
21 Q. Nobody disclosed to you what the
22 purpose of the study was for?
23 A. As best I can recall, but it's a
24 comparison between the immunogenicity between
25 two different vaccine doses, as best I can

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<p style="text-align: right;">Page 90</p> <p>1 recall, my understanding. 2 Q. Do you recall what those three 3 doses were? 4 A. No. 5 Q. Do you recall what the purpose 6 was behind those three doses were? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: All I recall is 10 that they were comparing the 11 immunogenicity of those three doses. I 12 don't recall further details. 13 BY MR. KELLER: 14 Q. So you don't know how that data 15 was going to be used? 16 A. I recall that there was going to 17 be a comparison of immunogenicity between 18 doses, but I don't recall details of how that 19 was going to be used. 20 Q. Did that comparison have any 21 clinical relevance to whether or not the 22 vaccine would protect a kid from getting sick 23 from mumps? 24 A. I don't -- I'm not -- it's 25 outside of my area of expertise. I don't know</p>	<p style="text-align: right;">Page 92</p> <p>1 that -- did you have any understanding that 2 the purpose of this assay was to identify an 3 end expiry potency for Merck's marketed MMR 4 product for the mumps component? 5 A. I recall that the title of the 6 study was an end expiry study. So that would 7 imply that an expiry was part of the study. 8 But I don't know, I don't recall how the data 9 factored into that calculation. 10 Q. When you say that you did 11 development work, can you describe for me what 12 you mean by development work? 13 MR. SANGIAMO: Object to the 14 form. 15 THE WITNESS: Just to clarify, 16 you're looking for, like, variables 17 that we are -- looked at in developing 18 the assay? 19 BY MR. KELLER: 20 Q. Sure. 21 A. So initial work was largely 22 based on any discussion with the FDA where we 23 ran options for the assay format, meaning 24 different virus strains, different supplements 25 to the media, different means of calculating</p>
<p style="text-align: right;">Page 91</p> <p>1 what the clinical -- connection for clinical 2 relevance was intended. 3 Q. Did you develop the assay for 4 Protocol 007? 5 MR. SANGIAMO: Objection. Form. 6 THE WITNESS: Other members of 7 the lab and I did development work to 8 develop the assay. It wasn't a -- 9 multiple people in the lab were 10 involved in the development of the 11 assay. 12 BY MR. KELLER: 13 Q. When you say "people in the 14 lab," people that worked for you, under you? 15 A. Everyone in the lab reported to 16 me, so yes. 17 Q. So when -- you say they helped 18 you run the experiments. Correct? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: In some cases, 22 helped design experiments and run 23 experiments. 24 BY MR. KELLER: 25 Q. At any time, did you understand</p>	<p style="text-align: right;">Page 93</p> <p>1 an endpoint, different means of visualizing 2 plaques. So in discussion with the FDA, we 3 presented data that we had from preliminary 4 experiments that we had conducted. Received 5 feedback from the FDA over their suggestions 6 of how to proceed in the assay development. 7 And then communicated results as we were 8 giving them to the FDA -- maybe not exactly 9 the day, but in a timely way from our 10 perspective to the FDA. And then identified 11 an assay format to move ahead for Protocol 12 007. 13 Q. When you say you got feedback 14 from the FDA, what do you mean by "feedback"? 15 A. Feedback meaning we presented 16 data, the FDA made suggestions, recommendations 17 of how to proceed. 18 Q. Did you understand those 19 suggestions and recommendations were binding 20 on the FDA? Did you understand that the FDA 21 was -- let me back up a second. We'll come 22 back to that in a moment. 23 So as you sit here today, you -- 24 strike that. 25 Is it fair to say that your</p>

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1 testimony is you don't know why Protocol 007
2 was being conducted?
3 A. As best I can recall, my
4 recollection and understanding was to compare
5 the immunogenicity of the three vaccine doses.
6 Q. Do you recall there being any
7 requirement by CBER -- you understand what
8 CBER is, right?
9 A. Yes.
10 Q. What's CBER?
11 A. Center for Biologics Evaluation
12 and Research.
13 Q. And they're a division of the
14 FDA. Correct?
15 A. Yes.
16 Q. And they specialize, for the
17 purposes of this case, in vaccine, correct,
18 biologics?
19 A. Biologics of vaccines, yes.
20 Q. So do you recall any
21 communications with the FDA or CBER where they
22 required for Protocol 007 that the assay be
23 linked to protection from disease?
24 MR. SANGIAMO: Object to the
25 form.

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1 THE WITNESS: I do not recall
2 any connection to protection.
3 BY MR. KELLER:
4 Q. If the assay was required to be
5 linked to protection from disease, would you
6 have developed a different assay?
7 MR. SANGIAMO: Object to the
8 form.
9 THE WITNESS: No.
10 BY MR. KELLER:
11 Q. You would have ran the same
12 assay?
13 A. My personal opinion is that the
14 protection from disease and antibody assay are
15 independent events. I would not have
16 automatically or wouldn't automatically
17 consider a different assay as more predictive
18 of protection versus another.
19 Q. So is it your belief that -- I'm
20 trying to understand that answer. You don't
21 believe that any assay that can be developed
22 is any more predictive of protection from
23 disease than any other? Is that your
24 testimony?
25 MR. SANGIAMO: Object to the

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1 form.
2 THE WITNESS: My opinion is that
3 the -- my understanding and opinion is
4 that the -- an antibody assay is an
5 imperfect model, imperfect measure of
6 an immune response to a vaccine. It's
7 not a given correlate of protection.
8 The assay itself is not -- does not
9 provide an automatic correlate of
10 protection.
11 BY MR. KELLER:
12 Q. Do you understand what a
13 surrogate of protection is?
14 A. I've heard of correlates of
15 protection. Surrogate I'm not sure about.
16 Q. You don't know what a surrogate
17 of protection is?
18 A. I've heard of correlate of
19 protection. Surrogate of protection, it's not
20 a familiar term to me.
21 Q. You said that antibody assays
22 are imperfect. Are any antibody assays more
23 relevant to a clinical link to protection than
24 others?
25 A. I can't -- I'm not an expert in

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1 the area of the -- of clinical as far as
2 making a comment on protection from disease.
3 My personal opinion is that none of -- at
4 least from my knowledge and experience, none
5 of the assays are an exact mimic of the immune
6 response that people would have.
7 Q. Right. But some assays are
8 better than others at predicting whether or
9 not a result from that assay is linked to a
10 clinical -- clinically relevant connection to
11 protection from disease?
12 A. I do not -- I don't agree with
13 that because I think it depends on the assay
14 format. For example, there may be some assays
15 that -- it would depend on the virus and the
16 disease.
17 Q. Let's talk about mumps.
18 A. Okay.
19 Q. Do you believe that -- you
20 understand what an ELISA assay is. Right?
21 A. I'm familiar with the format.
22 Q. You've never run an ELISA assay?
23 A. I have run ELISAs.
24 Q. Do you understand that an ELISA
25 assay is just a binding assay?

25 (Pages 94 - 97)

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<p style="text-align: right;">Page 98</p> <p>1 A. There are some versions of ELISA 2 that have functional activity, but the 3 majority of them are binding assays. 4 Q. Do you know what -- are you 5 familiar with the ELISA assay that was run in 6 Protocol 007? Let me strike that. 7 Do you understand that an ELISA 8 assay was run in Protocol 007? 9 A. I recall that an ELISA was run 10 as part of the Protocol 007 study. 11 Q. And did you ever review the 12 protocol for that ELISA assay? 13 MR. SANGIAMO: Object to the 14 form. 15 BY MR. KELLER: 16 Q. Let me strike that. 17 Do you recall whether or not a 18 protocol was developed for that ELISA assay 19 using Protocol 007? 20 MR. SANGIAMO: Object to the 21 form. 22 THE WITNESS: I don't know. 23 BY MR. KELLER: 24 Q. You don't know. Do you recall 25 ever reviewing a protocol for the ELISA</p>	<p style="text-align: right;">Page 100</p> <p>1 correlate. 2 BY MR. KELLER: 3 Q. Do you know whether or not Merck 4 ever correlated its plaque reduction 5 neutralization assay to an ELISA assay? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: I am aware of a 9 correlation that was done as part of -- 10 as best I can recall, Protocol 007, the 11 ELISA and the AIGENT assay. 12 BY MR. KELLER: 13 Q. Do you recall -- what do you 14 mean -- what's your understanding of the 15 correlation that was conducted as part of the 16 Protocol 007? 17 A. I don't have any details on how 18 the comparison was done. 19 Q. Were you involved in that at 20 all? 21 A. I can't exclude that I might 22 have received some e-mails about it, but I was 23 not involved in the planning of it or, as far 24 as I can recall, the exclusion other than the 25 neutralization part.</p>
<p style="text-align: right;">Page 99</p> <p>1 assay -- 2 MR. SANGIAMO: Object to the 3 form. 4 BY MR. KELLER: 5 Q. -- that was run -- used for 6 Protocol 007? 7 A. I don't recall reviewing the 8 protocol. 9 Q. Are you aware of whether or not 10 Merck has ever correlated its ELISA assay to 11 protection from disease? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: That's -- I don't 15 have experience in that area. So I 16 don't know. 17 BY MR. KELLER: 18 Q. Do you recall ever -- any 19 discussions about Merck's inability to 20 correlate its ELISA assay to a plaque 21 reduction neutralization assay? 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: I do not recall 25 any discussion of the inability to</p>	<p style="text-align: right;">Page 101</p> <p>1 Q. When did you first learn about 2 Protocol 007? 3 A. I don't recall a specific date. 4 Late '90s. I don't remember a specific date. 5 Q. Who told you about Protocol 007? 6 A. As best I can recall, at least 7 the person who comes to mind was Emilio Emini. 8 I can't say with certainty that he was the 9 first one who mentioned it, but he's the first 10 one that I recall. 11 Q. There was two SOPs for Protocol 12 007, wasn't there? 13 MR. SANGIAMO: Object to the 14 form. 15 BY MR. KELLER: 16 Q. Do you know what an SOP is? 17 A. I've seen SOPs, familiar with 18 the general format. 19 Q. Standard operation procedure? 20 A. Yes. 21 Q. Do you understand what an SOP is 22 with respect to an assay? 23 A. I'm familiar -- I understand 24 what its purpose is and what it includes for 25 the most part.</p>

26 (Pages 98 - 101)

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<p style="text-align: right;">Page 102</p> <p>1 Q. What is the purpose?</p> <p>2 A. The purpose is described the</p> <p>3 method of material, reagents, equipment that</p> <p>4 are needed, and in some cases the interpretation</p> <p>5 of the results.</p> <p>6 Q. You say interpretation of the</p> <p>7 results, how to calculate a result?</p> <p>8 A. What I'm thinking of there, for</p> <p>9 example, defining a negative result versus a</p> <p>10 positive result.</p> <p>11 Q. Seroclassification cutoff?</p> <p>12 Let's talk in particular about --</p> <p>13 MR. SANGIAMO: Wait a minute.</p> <p>14 You're withdrawing the last question?</p> <p>15 MR. KELLER: I'll withdraw the</p> <p>16 question.</p> <p>17 BY MR. KELLER:</p> <p>18 Q. When you learned about Protocol</p> <p>19 007, did you learn that you would be -- did</p> <p>20 anybody ask you to develop an assay for</p> <p>21 Protocol 007?</p> <p>22 A. Yes.</p> <p>23 Q. At that point, had an assay</p> <p>24 already been developed and you were asked to</p> <p>25 fine tune that assay or were you starting from</p>	<p style="text-align: right;">Page 104</p> <p>1 form.</p> <p>2 THE WITNESS: The purpose was to</p> <p>3 evaluate assay variables and see if any</p> <p>4 of them would allow us to have the</p> <p>5 capability of entering 95 percent</p> <p>6 seroconversion.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. That's what you did, isn't it?</p> <p>9 You developed that assay, didn't you?</p> <p>10 A. We developed in collaboration</p> <p>11 and discussion with the FDA.</p> <p>12 Q. You disclosed everything about</p> <p>13 that assay to the FDA. Is that your testimony?</p> <p>14 A. Yes.</p> <p>15 Q. Yes?</p> <p>16 A. Yes.</p> <p>17 Q. And so the FDA knew -- let me --</p> <p>18 we'll get to that.</p> <p>19 I just want to make sure,</p> <p>20 because you're under oath, you understand</p> <p>21 that. Correct?</p> <p>22 A. Yes.</p> <p>23 Q. So it's your testimony under</p> <p>24 oath that you disclosed every aspect of the</p> <p>25 assay to the FDA?</p>
<p style="text-align: right;">Page 103</p> <p>1 fresh?</p> <p>2 MR. SANGIAMO: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: There was a</p> <p>5 request to implement an assay that met</p> <p>6 a requirement that CBER imposed on the</p> <p>7 assay, and then as part of that</p> <p>8 implement was evaluation whether an</p> <p>9 existing assay was capable of providing</p> <p>10 that result, or assay, further assay</p> <p>11 development was required.</p> <p>12 BY MR. KELLER:</p> <p>13 Q. So was your -- what was that</p> <p>14 requirement?</p> <p>15 A. The requirement -- my</p> <p>16 understanding of the requirement was that CBER</p> <p>17 required a 95 percent seroconversion rate.</p> <p>18 Q. So you designed an assay to get</p> <p>19 a 95 percent seroconversion rate?</p> <p>20 A. Not to get a 95 percent</p> <p>21 seroconversion rate, but one that was capable</p> <p>22 of measuring a 95 percent seroconversion rate.</p> <p>23 Q. So was the purpose to define an</p> <p>24 assay that would get you that result?</p> <p>25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 105</p> <p>1 MR. SANGIAMO: Object to the</p> <p>2 form.</p> <p>3 THE WITNESS: My testimony is</p> <p>4 that I -- we provided available data on</p> <p>5 the effects of the variables, meaning</p> <p>6 different virus strains, supplements to</p> <p>7 the media, plaque utilization options.</p> <p>8 I can't exclude that there was some</p> <p>9 other factor aspect that we looked at</p> <p>10 that we didn't think was relevant or</p> <p>11 important to the key part of the</p> <p>12 discussion. So I can't exclude that</p> <p>13 some detail that I -- at least that</p> <p>14 I -- the best of my knowledge was not</p> <p>15 relevant was not disclosed to them. I</p> <p>16 can't say that it was not disclosed,</p> <p>17 but I can't exclude that there might</p> <p>18 not have been -- there might have been</p> <p>19 some aspect that we did not disclose.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. Do you recall when you learned</p> <p>22 about the Protocol 007, what type of an assay</p> <p>23 CBER was looking for?</p> <p>24 A. The requirement, as best I</p> <p>25 understand it, I was at the meeting, one of</p>

27 (Pages 102 - 105)

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1 the meetings with Cathy Carbone, is a CBER
 2 representative, one of the CBER
 3 representatives, she wanted a plaque reduction
 4 neutralization assay.
 5 Q. Are you sure that they didn't
 6 just ask for a functional neutralizing assay?
 7 They specifically said a plaque reduction
 8 neutralizing assay?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: The best of my
 12 recollection, it was a plaque reduction
 13 neutralization assay. I can't exclude
 14 that they might have used a different
 15 term, but my recollection, it was a
 16 plaque reduction neutralization assay.
 17 BY MR. KELLER:
 18 Q. Do you recall, in any of those
 19 communications with CBER, why CBER wanted a
 20 plaque reduction neutralization assay?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: I do not recall
 24 them, at least in my presence, giving
 25 an explanation of why.

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1 BY MR. KELLER:
 2 Q. Do you recall -- you don't -- as
 3 you sit here today right now, you don't recall
 4 ever hearing from CBER that they wanted a
 5 plaque reduction neutralization assay that
 6 could be clinically linked to protection from
 7 disease?
 8 A. I do not recall that -- a
 9 comment about a link to protection from
 10 disease.
 11 Q. Do you believe that an ELISA
 12 assay is just as good as a plaque reduction
 13 neutralization assay in terms of identifying
 14 whether or not a result from those assays is
 15 linked to protection from disease, from mumps?
 16 A. I would say -- I'm not familiar
 17 with the ELISA results either at Merck or
 18 outside of Merck to be able to comment on how
 19 well it correlates with protection from
 20 disease.
 21 Q. And that's not what you used to
 22 develop the assay, is trying to find an assay
 23 that would correlate to protection from
 24 disease. Correct?
 25 MR. SANGIAMO: Object to the

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1 form.
 2 THE WITNESS: For which assay?
 3 BY MR. KELLER:
 4 Q. The plaque reduction neutralization
 5 assay.
 6 A. The objective for the plaque
 7 reduction neutralization assay was to provide
 8 an assay that was capable of providing 95
 9 percent seroconversion. Whether that --
 10 beyond that, I don't have any understanding.
 11 Q. The plaque reduction neutralization
 12 assay -- let me strike that.
 13 We talked about SOPs. Did you
 14 draft an SOP for the plaque reduction
 15 neutralization assay?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: I don't recall if
 19 I did or someone else, another -- I
 20 don't recall if I was the author of the
 21 SOP or not.
 22 BY MR. KELLER:
 23 Q. Did you approve that SOP for the
 24 original plaque reduction neutralization
 25 assay -- strike that.

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1 When I say "plaque reduction
 2 neutralization assay," if I use PRN, you
 3 understand that to be the same?
 4 A. I'm sorry, PRN meaning the one
 5 used for Protocol 007? There are other plaque
 6 reduction neutralization assays that we've had
 7 in place.
 8 Q. Let's start with the one -- you
 9 start -- there was -- do you recall there
 10 being multiple SOPs for the neutralization
 11 assay that was used for Protocol 007?
 12 Correct?
 13 A. I recall two versions of it,
 14 yes.
 15 Q. And the first version, can you
 16 describe that assay to me? That was -- was
 17 that a PRN assay?
 18 A. Yes. Yes.
 19 Q. So when we say PRN throughout
 20 the rest of the deposition, we understand that
 21 to be a plaque reduction neutralization assay.
 22 Is that fair?
 23 A. Okay. Yeah. Well --
 24 Q. I know it changed.
 25 A. It's a plaque reduction

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<p style="text-align: right;">Page 110</p> <p>1 neutralization assay. 2 Q. You said there was two 3 versions -- another version. Did you prepare 4 that SOP? 5 A. Again, I don't recall if I was 6 the author of it. I just recall that there 7 was another version prepared. 8 Q. And that second version modified 9 the SOP from the first version. Correct? 10 A. The procedure did not -- it's my 11 understanding did not change -- the assay 12 procedure did not change. To the best of my 13 recollection, the changes in the revised 14 procedure were additional criteria for 15 specific, like, retests of samples or assays, 16 responses to flags from a workbook that was in 17 place. 18 Q. The first version, did the first 19 version that you worked on include antihuman 20 IgG? 21 A. For protocol -- the assay that 22 we used to start the testing of Protocol 007 23 included anti-IgG. 24 Q. Was there an assay before -- an 25 SOP before that?</p>	<p style="text-align: right;">Page 112</p> <p>1 MR. SANGIAMO: Object to the 2 form. 3 THE WITNESS: There were -- 4 there was a previous plaque reduction 5 neutralization assay not using anti-IgG 6 that had some common, some common 7 steps. So I -- my expectation is that 8 that was used as a template since some 9 of the steps were common -- I mean, 10 common cells, medium, overlay it, a 11 couple, various steps. So that would 12 have been used as a template for the 13 Protocol 007 development. 14 BY MR. KELLER: 15 Q. I see. 16 Who drafted that, I mean, that 17 other PRN that was used before the use of 18 anti-IgG step? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: I don't recall who 22 the author. 23 BY MR. KELLER: 24 Q. Did you run any experiments off 25 of that original PRN SOP?</p>
<p style="text-align: right;">Page 111</p> <p>1 MR. SANGIAMO: Object to the 2 form. 3 THE WITNESS: An assay for? 4 BY MR. KELLER: 5 Q. Strike that. 6 Was there an SOP for a PRN assay 7 that was run in the development of Protocol 8 007 before the AIGENT SOP? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: I'm sorry, I don't 12 understand. 13 BY MR. KELLER: 14 Q. Sure. You testified that you 15 understand that there's two different SOPs 16 written for Protocol 007, the PRN assay that 17 was used for Protocol 007. Correct? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: There were two 21 versions of the SOP for the AIGENT 22 assay used in Protocol 007. 23 BY MR. KELLER: 24 Q. Prior to the AIGENT assay, was 25 that developed from another SOP?</p>	<p style="text-align: right;">Page 113</p> <p>1 MR. SANGIAMO: Object to the 2 form. 3 THE WITNESS: We ran plaque 4 reduction assays with an assay without 5 anti-IgG. What I'm not remembering 6 with clarity is whether there was only 7 one plaque reduction neutralization 8 assay without anti-IgG. So there was a 9 plaque reduction neutralization assay 10 without anti-IgG that was used to test 11 in some testings. 12 BY MR. KELLER: 13 Q. When you were brought into the 14 project to work on Protocol 007, had 15 development work already been started -- 16 MR. SANGIAMO: Object to the 17 form. 18 BY MR. KELLER: 19 Q. -- for Protocol 007? 20 MR. SANGIAMO: Object to the 21 form. 22 THE WITNESS: That, I don't 23 know. 24 BY MR. KELLER: 25 Q. But you don't recall preparing</p>

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Page 114	<p>1 the SOP that used without the IgG step. 2 Correct? 3 A. I don't recall who the author. 4 There's an equal chance I wasn't the author, I 5 don't remember. 6 Q. Do you recall whether or not the 7 original PRN SOP before the anti-IgG step was 8 added, was that a -- considered a standard 9 bread and butter PRN assay? 10 MR. SANGIAMO: Object to the 11 form. 12 THE WITNESS: It's -- I don't 13 know the term "bread and butter," I 14 guess I would -- not clear on how to 15 respond to that. But it's an assay 16 format that others had or other labs 17 had used. 18 BY MR. KELLER: 19 Q. Had that assay -- do you know 20 what validation means of an assay? 21 A. I'm familiar with some aspects 22 to it. 23 Q. Have you ever -- do you know 24 what a validation protocol is? 25 A. I've seen validation protocols</p>	Page 116	<p>1 MR. SANGIAMO: Object to the 2 form. 3 MR. KELLER: Let me strike that. 4 BY MR. KELLER: 5 Q. Did you draft the validation 6 protocol for the AIGENT SOP that was used for 7 Protocol 007? 8 MR. SANGIAMO: Object to the 9 form. 10 THE WITNESS: I don't -- I do 11 recall drafting a document that 12 included aspects of the validation. I 13 don't consider that to be the protocol 14 itself, but -- and I don't recall 15 drafting the formal protocol. 16 BY MR. KELLER: 17 Q. Do you know who did? 18 A. I know who issued the report on 19 it. I don't know who -- I don't recall who 20 drafted it. 21 Q. Do you understand the difference 22 between a validation report and a validation 23 protocol? 24 A. I can't say -- I don't have 25 confidence of what -- how they relate.</p>
Page 115	<p>1 for assays. I don't know if there's 2 validation for assays for other things. But 3 for protocols of assays, I have seen them. 4 Q. Have you ever validated an assay 5 yourself? 6 A. I've been involved in assay 7 validation. 8 Q. Have you ever validated a plaque 9 reduction neutralization assay before? 10 MR. SANGIAMO: Object to the 11 form. 12 THE WITNESS: I was -- or did 13 part of the work for validation of a 14 plaque reduction neutralization assay. 15 BY MR. KELLER: 16 Q. And that was part of Protocol 17 007? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: There was a 21 validation protocol done, assay 22 protocol done for Protocol 007 which I 23 did contribute to. 24 BY MR. KELLER: 25 Q. Did you draft that protocol?</p>	Page 117	<p>1 Q. Have you ever been trained in 2 any way on validating an assay in terms of the 3 steps that are required? 4 A. I have consulted with our, for 5 example, our biometrics group on what is 6 required for the validation study. Whether 7 that constitutes training, I can't comment. 8 Q. Who did you -- and that's for 9 Protocol 007? Strike that. 10 Did you confer with -- the 11 person that you conferred with for -- from 12 biometrics research for validating an assay, 13 was that for Protocol 007? 14 A. That's an example where a 15 biometrics person was consulted. 16 Q. The biometrics person, is that a 17 statistician? 18 A. That's my genericized view of 19 them. I don't -- I can't say with certainty 20 what their full background is. 21 Q. So have you ever drafted a 22 validation protocol prior to Protocol 007? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: Again, I don't</p>

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<p style="text-align: right;">Page 118</p> <p>1 recall if -- I remember preparing a 2 document, whether it was a protocol or 3 not, but there was a series of them 4 before Protocol 007. 5 BY MR. KELLER: 6 Q. Let's start before Protocol 007. 7 Have you ever validated an assay 8 where you were required to draft the 9 validation protocol for that assay? 10 A. Again, with the reservation of 11 the term validation protocol. I'm not sure if 12 whatever I drafted was a protocol, but -- 13 Q. Let's start from the beginning. 14 MR. SANGIAMO: Wait a minute. 15 You have to let him finish the 16 question -- 17 MR. KELLER: Sure. 18 MR. SANGIAMO: -- finish the 19 answer. 20 THE WITNESS: So there are other 21 assays for which I have contributed to 22 a validation study. Whether the 23 document that I -- document or 24 documents I prepared were a formal 25 validation protocol or just an outline</p>	<p style="text-align: right;">Page 120</p> <p>1 MR. SANGIAMO: Object to the 2 form. 3 THE WITNESS: Yes. 4 BY MR. KELLER: 5 Q. Were those used to -- do you 6 recall what that product was? 7 A. It was a comparison between MMR 8 and Priorix. 9 Q. Other than that -- that was 10 Protocol 006, do you recall that? 11 A. Yes. 12 Q. Other than Protocol 006, had you 13 ever run any clinical samples? 14 A. Yes. 15 MR. SANGIAMO: Object to the 16 form. 17 BY MR. KELLER: 18 Q. When would that happen? 19 A. That was in -- I don't remember 20 the exact date, but it was a mid -- in the 21 1990s. I was going to say mid-1990s, but I 22 don't recall specifically. 23 Q. When you ran those clinical 24 studies in the 1990s, do you recall whether or 25 not you ran those studies in accordance with</p>
<p style="text-align: right;">Page 119</p> <p>1 of what was being done, I can't say. I 2 don't recall. 3 BY MR. KELLER: 4 Q. Was Protocol 007 a clinical 5 study? 6 A. That was a clinical study. 7 Q. Was it a Phase III study? 8 A. I don't recall what the phase 9 is. I have an expectation just based on just 10 general exposure to clinical studies, but it 11 would be a guess. 12 Q. Do you know whether or not 13 Protocol 007 was a pivotal study? Let me 14 strike that. 15 Do you know what a pivotal study 16 is? 17 A. No. 18 Q. Had you ever run clinical 19 samples with human sera in your lab prior to 20 Protocol 007? 21 MR. SANGIAMO: Objection. Form. 22 THE WITNESS: Yes. 23 BY MR. KELLER: 24 Q. Were those used for a marketed 25 product?</p>	<p style="text-align: right;">Page 121</p> <p>1 the rules of current GMP? 2 MR. SANGIAMO: Object to the 3 form. 4 THE WITNESS: Well, they were 5 not clinical studies, they were 6 clinical samples. They were -- as best 7 as I understand, they were not run 8 under GMP requirements, nor did we 9 expect that they needed to be run under 10 GMP. 11 BY MR. KELLER: 12 Q. Protocol 006, did you understand 13 that had to be run under GMP? 14 A. My understanding was that it did 15 not. 16 Q. Did you understand that Protocol 17 007 had to be? 18 A. No. 19 Q. Where did you gain that 20 understanding from, that it didn't have to be 21 run under GMP? 22 MR. SANGIAMO: Object to the 23 form. 24 BY MR. KELLER: 25 Q. Strike that.</p>

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<p style="text-align: right;">Page 122</p> <p>1 Where did you learn that</p> <p>2 Protocol 007 did not have to be run under GMP</p> <p>3 studies?</p> <p>4 A. Management had -- no one had</p> <p>5 made any indication in the assay development</p> <p>6 discussions that it was required to be run</p> <p>7 under GMP conditions. I'm sorry, qualify that</p> <p>8 up and to the point of the FDA inspection.</p> <p>9 Q. After the FDA inspected in</p> <p>10 August of 2001, is that the first time that</p> <p>11 you learned that Protocol 007, the assays that</p> <p>12 you ran were supposed to be run under GMP</p> <p>13 conditions?</p> <p>14 MR. SANGIAMO: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: That was the first</p> <p>17 I heard of the expectation that the</p> <p>18 assays were run under GMP conditions.</p> <p>19 MR. KELLER: Let me do this.</p> <p>20 Let me mark as Exhibit 20.</p> <p>21 - - -</p> <p>22 (Exhibit Krah-20, 3/15&16/1999</p> <p>23 MMR II Mumps Expiry Study Investigators</p> <p>24 Meeting Agenda, 17644 - 17666, was</p> <p>25 marked for identification.)</p>	<p style="text-align: right;">Page 124</p> <p>1 that refers to.</p> <p>2 Q. Under -- in the first page of</p> <p>3 the agenda it identifies Dr. Scott Thaler. Do</p> <p>4 you see that?</p> <p>5 A. Yes.</p> <p>6 Q. It identifies him as a clinical</p> <p>7 monitor. Do you see that?</p> <p>8 A. Yes.</p> <p>9 Q. Do you understand what a</p> <p>10 clinical monitor is in a clinical study?</p> <p>11 A. I have a very general</p> <p>12 understanding of it, but not -- I don't have</p> <p>13 any details or a full understanding of what</p> <p>14 that person's responsibilities are.</p> <p>15 Q. What's your understanding?</p> <p>16 A. For one to -- perhaps adding a</p> <p>17 little -- someone who monitors the clinical --</p> <p>18 the progress -- the design and actually -- and</p> <p>19 progress of the clinical study. That's just</p> <p>20 my personal, the way I frame what the</p> <p>21 responsibility is. But, again, what that</p> <p>22 really means -- what the roles are, what they</p> <p>23 actually do, I don't know.</p> <p>24 Q. Fair enough. If you look under</p> <p>25 the attendees, it has Ms. Yagodich was also an</p>
<p style="text-align: right;">Page 123</p> <p>1 - - -</p> <p>2 MR. KELLER: For the record,</p> <p>3 Exhibit 20 is a document that bears</p> <p>4 Bates stamp number 17644 through 66,</p> <p>5 and it's an agenda for a March 15 and</p> <p>6 16, 1999 investigator's meeting, MMR II</p> <p>7 mumps expiry study.</p> <p>8 BY MR. KELLER:</p> <p>9 Q. Sir, can you tell me, if you</p> <p>10 recall, seeing this document before? And I</p> <p>11 will direct your attention to 17646 where it</p> <p>12 identifies the Merck attendees, and you are</p> <p>13 identified as one of the attendees of this</p> <p>14 particular meeting.</p> <p>15 A. I don't recall this. I do see</p> <p>16 my name there as a Merck attendee, but I don't</p> <p>17 recall it.</p> <p>18 Q. Do you have any reason to</p> <p>19 believe you didn't attend?</p> <p>20 A. If they have me listed as an</p> <p>21 attendee, I would take that to mean that I did</p> <p>22 attend.</p> <p>23 Q. This MMR mumps expiry study, do</p> <p>24 you understand it to be Protocol 007?</p> <p>25 A. That's my understanding of what</p>	<p style="text-align: right;">Page 125</p> <p>1 attendee. Do you see that?</p> <p>2 A. Yes.</p> <p>3 Q. This is an investigator's</p> <p>4 meeting. Do you understand what investigators</p> <p>5 -- do you understand what the purpose of this</p> <p>6 meeting was?</p> <p>7 A. I don't recall, no.</p> <p>8 Q. Do you know what an investigator</p> <p>9 is?</p> <p>10 A. I know what an investigator is.</p> <p>11 Q. What is an investigator?</p> <p>12 A. And investigator is someone who</p> <p>13 is going to be taking part in a clinical</p> <p>14 study.</p> <p>15 Q. Were you an investigator for</p> <p>16 Protocol 007?</p> <p>17 A. No, my understanding -- maybe</p> <p>18 qualify the investigator, that my</p> <p>19 understanding is it's an external person who</p> <p>20 is involved in the clinical study execution in</p> <p>21 the field. I don't consider myself an</p> <p>22 investigator in the context of the investigator's</p> <p>23 meeting.</p> <p>24 Q. I see.</p> <p>25 For purposes of running clinical</p>

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<p style="text-align: right;">Page 126</p> <p>1 studies that you ran in your lab, do you 2 consider yourself an investigator for that 3 function? 4 MR. SANGIAMO: Object to the 5 form. 6 THE WITNESS: I was a research 7 scientist supporting the studies. 8 Whether one calls that an investigator, 9 I wouldn't specifically term or phrase 10 it as an investigator. 11 BY MR. KELLER: 12 Q. Do you know what a sponsor is in 13 a clinical study? 14 A. I don't have a full understanding 15 of it. It would be a guess of what that means. 16 Q. You don't know? 17 A. No. 18 Q. Here Mary Yagodich was also an 19 attendee. Do you know why she would have 20 attended an investigator's meeting for 21 Protocol 007? 22 A. I can't say with certainty. 23 Q. Who is Timothy Schofield? 24 A. Timothy Schofield was listed 25 here as someone in the biometrics research.</p>	<p style="text-align: right;">Page 128</p> <p>1 - - - 2 (Exhibit Krah-21, PowerPoint 3 presentation, 17605 - 17612, was marked 4 for identification.) 5 - - - 6 BY MR. KELLER: 7 Q. I'll represent to you that these 8 documents all came from a single file. 9 Exhibit 21 is a document that bears Bates 10 stamp number 17605 through 17612. 11 Sir, can you tell me if you 12 recall seeing this document before, and if you 13 recognize any of the handwriting on this 14 document? 15 MR. SANGIAMO: Dr. Krah, make 16 sure you're clear on your answer, what 17 you're saying yes or no to. 18 MR. KELLER: Strike that 19 question. 20 BY MR. KELLER: 21 Q. Sir, can you tell me if you 22 recognize the handwriting on 17611? 23 A. I do not. 24 Q. Do not. That's not your 25 handwriting?</p>
<p style="text-align: right;">Page 127</p> <p>1 So my generic description is that he's a 2 statistician. I don't recall what his role 3 was in the overall statistics evaluation. 4 Q. You testified earlier that you 5 conferred with somebody in biometric research 6 regarding the validation of the AIGENT? 7 A. Yes. 8 Q. Is that who you conferred with? 9 A. I can't say with certainty that 10 he wasn't the person. The person I was 11 thinking of was someone else. 12 Q. And Dr. Thaler was at this 13 meeting as well. Correct? 14 A. He's listed here as being one of 15 the attendees. 16 Q. There's three people from MPC. 17 Do you know what that represents? 18 A. I don't recall what that stands 19 for. 20 Q. There's also a Susan McNeill 21 from clinical quality assurance. Do you know 22 what her job responsibilities were? 23 A. I don't. 24 MR. KELLER: Let me mark this 25 next exhibit as Exhibit 21.</p>	<p style="text-align: right;">Page 129</p> <p>1 A. No, it's not my handwriting. 2 Q. If you look on the -- do you 3 recall seeing this document before? 4 A. It doesn't -- I don't -- it 5 doesn't look familiar to me. I don't recall 6 seeing it before. 7 Q. Under the third -- this is a 8 PowerPoint presentation document. Do you 9 recognize the format? 10 A. It looks like a PowerPoint 11 presentation. 12 Q. And the third -- the third slide 13 on the first page, it identifies Merck 14 personnel, and you're identified there along 15 with Ms. Yagodich. Do you see that? 16 A. Yes. 17 Q. Do you -- are you familiar with 18 Ms. Yagodich's handwriting? 19 A. Yes. 20 Q. Do you recognize that to be the 21 handwriting of Ms. Yagodich's at 17611? 22 A. That does not -- at least it's 23 my recollection, does not look like her 24 handwriting. 25 Q. Do you have any reason to</p>

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<p style="text-align: right;">Page 130</p> <p>1 believe that you didn't receive this document 2 as part of your -- the meeting that happened 3 on March 15th and 16th -- 4 MR. SANGIAMO: Object to the 5 form. 6 BY MR. KELLER: 7 Q. -- regarding the Protocol 007 8 investigator's meeting? 9 MR. SANGIAMO: Object to the 10 form. You can answer. 11 THE WITNESS: I don't have any 12 recollection of seeing it. I can't -- 13 I don't recall that this was handed out 14 at the meeting. I have no recollection 15 of it. 16 BY MR. KELLER: 17 Q. You don't recall? 18 A. No. 19 Q. You don't recall going to a 20 meeting where Protocol 007 was discussed to 21 the investigators of the clinical study? 22 A. I don't -- yeah, I don't recall 23 that. 24 Q. Let me turn your attention to 25 17607 in the second slide. It says the</p>	<p style="text-align: right;">Page 132</p> <p>1 says, "The FDA (CBER) has requested expiry 2 potencies be placed on the label of MMR II." 3 Do you see that? 4 A. Yes. 5 Q. Is this the first time you're 6 learning that -- 7 MR. SANGIAMO: Object to the 8 form. 9 BY MR. KELLER: 10 Q. -- today? 11 MR. SANGIAMO: Object to the 12 form. 13 MR. KELLER: Let me strike that. 14 BY MR. KELLER: 15 Q. Did you have that understanding 16 of -- of this statement? 17 MR. SANGIAMO: Wait until he 18 finishes. I'm sorry, what's your 19 question? 20 MR. KELLER: I'll rephrase it. 21 BY MR. KELLER: 22 Q. Do you recall ever hearing that 23 statement before? 24 A. I can't -- I don't recall. 25 Q. You don't recall. So you don't</p>
<p style="text-align: right;">Page 131</p> <p>1 "BACKGROUND AND RATIONALE." 2 Do you see that? 3 A. Yes. 4 Q. The first bullet point, it says, 5 The components of the MMR II are live viruses 6 and lose potency over time when stored at 2 to 7 8 degrees Celsius or higher. 8 Do you see that? 9 A. Yes. 10 Q. Do you recall ever -- do you 11 have any reason to believe that statement was 12 untrue? 13 A. All I can say is a generic 14 statement that live viruses lose potency over 15 time. So the statement about live vaccines 16 that lose potency over time are stored at 2 to 17 8 or higher. I have no reason to question 18 that statement. 19 Q. Do you recall learning that as 20 part of your development -- strike that. 21 Do you recall learning that 22 statement as part of your work on Protocol 23 007? 24 A. No. 25 Q. No. The second bullet point it</p>	<p style="text-align: right;">Page 133</p> <p>1 recall participating in this meeting, but you 2 have no reason to believe you didn't 3 participate. Correct? 4 A. My name is listed as an 5 attendee. Just I don't have any memory of the 6 meeting. 7 Q. You don't recall traveling to 8 Texas; Irving, Texas? 9 A. I don't. 10 Q. Have you ever been to Irving, 11 Texas? 12 A. I've been in Texas. I don't 13 recall what the meeting -- 14 Q. Have you ever been to the Omni 15 Mandalay Hotel? It's a nice hotel. 16 A. I recall being at the Omni in 17 Atlanta. I don't recall the Omni in Irving. 18 Q. So you don't recall ever learning 19 that CBER required that end expiry potencies 20 be placed on the label? 21 A. I'm sorry, did I ever? I 22 didn't -- I'd say, yes. I don't -- I'm not 23 that familiar with the label or what goes in 24 the label to be able to say that that is 25 expected.</p>

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1 Q. So you don't know?

2 A. I don't know.

3 Q. The next bullet point says, "No

4 data exist for mumps at the expiry potency

5 Merck has selected."

6 Do you see that?

7 A. Yes.

8 Q. In the next slide, it identifies

9 "MMR II END EXPIRY POTENCIES SUGGESTED FOR THE

10 LABEL Mumps 3.7."

11 Do you see that?

12 A. I'm sorry.

13 Q. The third slide on this page.

14 A. Oh, okay.

15 Q. Is that a fair representation of

16 that statement?

17 MR. SANGIAMO: Object to the

18 form.

19 MR. KELLER: Strike that.

20 BY MR. KELLER:

21 Q. Is that a fair representation of

22 that slide?

23 A. It says that the end expiry

24 potency suggests that the label for mumps is

25 3.7 TCID50 per dose.

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1 Q. So are you aware that Merck had

2 no data for mumps at end expiry of 3.7 --

3 MR. SANGIAMO: Object to the

4 form.

5 BY MR. KELLER:

6 Q. -- at this time frame?

7 MR. SANGIAMO: Objection. Form.

8 THE WITNESS: I don't recall

9 that lack of data.

10 BY MR. KELLER:

11 Q. Sir, I'm going to show you what

12 is marked as Exhibit 3, Bates page 488502,

13 page 98, dated Tuesday, March 16, 1999. Can

14 you tell me if that -- if your journal

15 references you participating in this

16 investigator's meeting on March 15 and 16,

17 1999?

18 A. Let's see. So it lists the

19 mumps expiry file clinical investigator's

20 meeting in Dallas, Texas and has a check mark

21 next to it which implies -- the check mark

22 implies that that happened.

23 Q. Does that lead you to believe

24 that you actually went and participated at

25 this particular meeting?

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1 A. So I can't say with certainty

2 that that check mark means I attended. The

3 PowerPoint presentation has me listed -- not

4 the PowerPoint. The slides have me listed as

5 an attendee, but the check mark, and the only

6 reason I'm saying that is, I may not

7 necessarily mean that, because I don't --

8 there are some meetings for which I might have

9 called in or taken part in part of the meeting

10 but not physically been there and I might have

11 still put a check mark.

12 Q. That would mean that you had

13 participated, you may not have been there

14 physical present, you may have done it on the

15 phone?

16 A. Yes. It may have been on the

17 phone, may have been -- included a subset of

18 the presentation.

19 Q. So if you go back to Exhibit 21,

20 in the second slide, the last bullet point

21 says, "A clinical immunogenicity trial is

22 necessary to provide these data."

23 Do you see that?

24 MR. SANGIAMO: I'm sorry. You

25 said second slide?

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1 BY MR. KELLER:

2 Q. 17607, the second slide, the

3 last bullet point, do you see that?

4 A. The fourth bullet point on the

5 second slide --

6 Q. Yes.

7 A. -- you have "clinical

8 immunogenicity trial is necessary to provide

9 the data." Yes.

10 Q. Does that refresh your memory

11 that the purpose of Protocol 007 was to try to

12 establish that a potency of 3.7 would be used

13 as the end expiry on the label for the mumps

14 component of MMR II?

15 A. It does not. Again, my

16 recollection is that this was comparing three

17 different vaccine doses. I don't have a

18 recollection of which was -- what those three

19 were or what the implications were.

20 Q. Was 3.7 one of the doses that

21 you were testing?

22 A. I don't recall. I recall there

23 were three doses, but I don't remember what

24 the doses were.

25 Q. Let me direct your attention to

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<p style="text-align: right;">Page 138</p> <p>1 17611, in particular to the last slide. 2 MR. SANGIAMO: You're asking a 3 lot of questions about this document. 4 I don't think he's had a chance to 5 review the whole document yet. Dr. 6 Krah, certainly feel free to read the 7 document. 8 MR. KELLER: Could we off the 9 record? 10 MR. SANGIAMO: It's not going to 11 take long. Stay on the record. 12 BY MR. KELLER: 13 Q. Let me know when you're done. 14 A. Okay. 15 MR. KELLER: Back on the record. 16 MR. SANGIAMO: Yes. Never went 17 off. 18 BY MR. KELLER: 19 Q. Sir, you've had a chance to 20 review every slide on Exhibit 21. Do any of 21 these slides refresh your recollection that 22 you've seen these slides before or this 23 presentation? 24 A. No. Nothing -- 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 140</p> <p>1 circular. So the purpose of the plaque 2 reduction neutralization assay would be to -- 3 or a plaque reduction assay would be to show 4 that antibodies are capable of binding to the 5 virus and causing it to be less capable of 6 forming -- of infecting and replicating in 7 cell culture. 8 Q. And so the antibodies that 9 you -- strike that. 10 Are there any other functional 11 neutralization assays other than a plaque 12 reduction neutralization assay? 13 A. There may be. Plaque reduction 14 is the one I'm most familiar with. Yes, there 15 are. 16 Q. The one you're most familiar 17 with is the PRN. Correct? 18 A. Yes. 19 Q. Do you know what a CPE assay is? 20 A. I'm familiar with the term. 21 Q. Ever run one? 22 A. Yes. 23 Q. Is that a functional assay as 24 well? 25 A. It's a -- when I said ran CPE</p>
<p style="text-align: right;">Page 139</p> <p>1 form. 2 THE WITNESS: Nothing looks 3 familiar. 4 BY MR. KELLER: 5 Q. Let me direct your attention to 6 17611, see if I can't refresh your memory of 7 this time frame. Under "IMMUNOGENICITY 8 MEASUREMENTS," do you see that? 9 A. Yes. 10 Q. In the second bullet point it 11 says, "For Mumps, a functional (neutralization) 12 assay has been developed." 13 Do you see that? 14 A. Yes. 15 Q. What do you understand functional 16 to mean? 17 A. To me it means a plaque 18 reduction neutralization assay. That's my 19 personal interpretation of that. That it's 20 showing a reduction in infectivity. 21 Q. When you say "reduction in 22 infectivity," you're -- can you describe that 23 a little bit for me? What are you testing to 24 show reduction infectivity? 25 A. Phrase this so it's not</p>	<p style="text-align: right;">Page 141</p> <p>1 assays, I ran assays to monitor cytopathic 2 effects in the titer virus, not in a 3 neutralization format. But it -- I would say 4 an assay such as a CPE reduction would be a 5 measure of the capacity of an antibody to 6 reduce infectivity so that -- I guess, one 7 could also call it a functional assay. 8 Q. When you're talking about an 9 antibody, let's talk about it in -- let's pick 10 one antibody. Let's talk about mumps. In a 11 mumps plaque reduction neutralizing assay, are 12 you looking for any antibody that's capable of 13 binding to a mumps virus or are you looking 14 for something else? 15 MR. SANGIAMO: Object to the 16 form. 17 MR. KELLER: Let me strike that. 18 BY MR. KELLER: 19 Q. In the plaque reduction 20 neutralization assay using a mumps vaccine, 21 can you describe for me how that's run? 22 MR. SANGIAMO: Object to the 23 form. 24 BY MR. KELLER: 25 Q. You take serum. Correct?</p>

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<p style="text-align: right;">Page 142</p> <p>1 A. Yes.</p> <p>2 Q. From a kid before they're</p> <p>3 vaccinated. Correct?</p> <p>4 A. Typically.</p> <p>5 MR. SANGIAMO: Object to this</p> <p>6 line of questioning. Keep going.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. Let me -- for Protocol 007, did</p> <p>9 the plaque reduction neutralizing assay you</p> <p>10 ran in that assay, you understood that you</p> <p>11 took kids before they were vaccinated,</p> <p>12 correct, you took their blood?</p> <p>13 A. There was a serum before</p> <p>14 vaccination.</p> <p>15 Q. And then you wait a certain</p> <p>16 number of days and then you took -- the kid is</p> <p>17 vaccinated and you wait a certain number of</p> <p>18 days after vaccination and you take the kid's</p> <p>19 blood after vaccination. Correct?</p> <p>20 MR. SANGIAMO: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: The serum is drawn</p> <p>23 before vaccination and then some</p> <p>24 interval after vaccination.</p> <p>25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 144</p> <p>1 Q. It has to be mumps specific?</p> <p>2 A. Yes.</p> <p>3 Q. If it's not mumps specific,</p> <p>4 would that be a problem?</p> <p>5 MR. SANGIAMO: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: If it's not mumps</p> <p>8 specific, that difference in specificity</p> <p>9 would need to be considered.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Why would it need to be</p> <p>12 considered?</p> <p>13 A. It depends on how to interpret</p> <p>14 what it means.</p> <p>15 Q. So if -- what does specificity</p> <p>16 mean? Can you describe that for me?</p> <p>17 A. My interpretation of specificity</p> <p>18 is uniqueness of the -- in the case of an</p> <p>19 antibody, its ability to bind or neutralize a</p> <p>20 virus, meaning that an antibody to one virus</p> <p>21 won't neutralize another virus.</p> <p>22 Q. So if a virus other than mumps</p> <p>23 would bind -- strike that.</p> <p>24 If an antibody other than a</p> <p>25 mumps antibody were to bind to the virus and</p>
<p style="text-align: right;">Page 143</p> <p>1 Q. And in the plaque reduction</p> <p>2 neutralization assay you're comparing those</p> <p>3 two blood samples. Correct?</p> <p>4 A. That's part of the evaluation.</p> <p>5 Q. So in -- just so I understand</p> <p>6 how this process works, you take -- you're</p> <p>7 looking for, in the pre-vaccination sample to</p> <p>8 see whether or not the kid has mumps</p> <p>9 neutralizing antibodies. Correct?</p> <p>10 A. Yes.</p> <p>11 Q. Are you looking to see whether</p> <p>12 or not the kid has any antibodies that will</p> <p>13 neutralize the mumps virus?</p> <p>14 MR. SANGIAMO: Object to the</p> <p>15 form.</p> <p>16 THE WITNESS: My understanding</p> <p>17 is that we're looking for antibodies</p> <p>18 that are capable of binding to a</p> <p>19 neutralizing virus.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. That could be any antibodies,</p> <p>22 whether it's mumps antibodies or any other</p> <p>23 antibodies. Correct?</p> <p>24 A. It would have to be mumps</p> <p>25 specific.</p>	<p style="text-align: right;">Page 145</p> <p>1 neutralize it, that would be part of an</p> <p>2 analysis of specificity. Correct?</p> <p>3 MR. SANGIAMO: Object to the</p> <p>4 form.</p> <p>5 THE WITNESS: From my</p> <p>6 understanding, an evaluation of</p> <p>7 specificity could include or amongst</p> <p>8 other options looking for ability or</p> <p>9 capacity of antibodies unrelated to</p> <p>10 mumps to bind and neutralize.</p> <p>11 BY MR. KELLER:</p> <p>12 Q. Why would that be important in a</p> <p>13 plaque reduction neutralization assay that was</p> <p>14 run for Protocol 007 -- strike that.</p> <p>15 Was that important for -- to</p> <p>16 determine the specificity of nonspecific</p> <p>17 binding in the Protocol 007 assay?</p> <p>18 A. I'm not sure I understand your</p> <p>19 question.</p> <p>20 Q. Let me rephrase it if you don't</p> <p>21 understand it. As part of Protocol 007</p> <p>22 validation, did you investigate whether or</p> <p>23 not -- what the specificity of that assay was?</p> <p>24 A. Yes.</p> <p>25 Q. And you looked at -- what did</p>

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<p style="text-align: right;">Page 146</p> <p>1 you look at to determine the specificity of 2 that assay? 3 A. As best I recall, we had lab 4 volunteer sera, meaning sera from adult lab 5 volunteers, that then were absorbed with 6 measles, mumps, or rubella antigens or just 7 diluted in culture medium. And then the 8 residual neutralizing capacity of that -- 9 those sera were tested. 10 Q. And do you recall the results of 11 that? 12 A. I don't recall all the specific 13 results, but as a general recollection -- 14 Q. What's your general recollection? 15 A. General recollection was that 16 the antibody titers were reduced more by mumps 17 absorption than by measles or rubella 18 absorption. 19 Q. And so did you ever come to a 20 conclusion as to what the specificity of that 21 assay was based on those experiments you ran? 22 A. So I have a personal conclusion 23 that I reached -- 24 Q. Sure. 25 A. -- which was that the assay was</p>	<p style="text-align: right;">Page 148</p> <p>1 form. 2 THE WITNESS: That's not my 3 interpretation. 4 BY MR. KELLER: 5 Q. Did you ever come up with a 6 percentage of specificity? 7 A. No. 8 Q. Did anybody ever discuss the 9 percentage of specificity? 10 A. No, and I never actually heard 11 that. 12 Q. Did you ever test -- you never 13 heard that the assay was only 50 percent 14 specific to mumps specific antibodies? 15 A. What I recall seeing was that 16 for half of the sera tested, there was 17 absorption of some of the sera with other 18 antigens other than mumps. 19 Q. That was measles and rubella. 20 Correct? 21 A. I don't know that it was both of 22 them. I do recall rubella giving some -- 23 absorbing with rubella reduced the neutralizing 24 titers for some of the sera. But for some of 25 the -- some number of the sera, the absorption</p>
<p style="text-align: right;">Page 147</p> <p>1 specific. Those data were shared with others 2 at Merck and with the FDA and with -- I never 3 received any feedback to the contrary. 4 Q. Did you understand that the 5 rubella virus was also neutralizing, the mumps 6 virus in the PRN assay? 7 A. I'm sorry, your question is -- 8 Q. Sure. Did you understand that 9 the rubella had neutralizing impact on the PRN 10 assay? 11 MR. SANGIAMO: Object to the 12 form. 13 MR. KELLER: Let me strike that. 14 BY MR. KELLER: 15 Q. Do you recall that the rubella 16 antibodies were having a neutralizing effect 17 on the PRN assay that was tested by your lab? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: That is not my 21 interpretation of the data. 22 BY MR. KELLER: 23 Q. What about the measles? 24 A. No. 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 149</p> <p>1 was much greater for mumps antigen. 2 Q. Do you recall that -- 3 MR. SANGIAMO: Jeff, we've been 4 going about an hour and 20 minutes. 5 MR. KELLER: Why don't I finish 6 this line of question. 7 BY MR. KELLER: 8 Q. Do you recall that the control 9 medium was also neutralizing the mumps virus 10 as part of the specificity assay? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: It was not 14 neutralizing. 15 BY MR. KELLER: 16 Q. Did you ever consider testing 17 whether or not the use of the rabbit anti-IgG 18 was, in fact, causing neutralization in and of 19 itself? 20 A. Yes. 21 Q. How did you do that? 22 A. By incubating the virus with the 23 anti-IgG in the absence of serum. 24 Q. Did you try it with serum? 25 A. Yes, I --</p>

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1 Q. Was there interaction --
 2 MR. SANGIAMO: Whoa, whoa, whoa.
 3 Hold on.
 4 BY MR. KELLER:
 5 Q. Finish your answer.
 6 MR. SANGIAMO: The question is
 7 did you try it with serum?
 8 THE WITNESS: Yes.
 9 BY MR. KELLER:
 10 Q. And did you -- you ran
 11 experiments with serum and anti-IgG and virus
 12 without mumps antibodies --
 13 MR. SANGIAMO: Object to the
 14 form.
 15 BY MR. KELLER:
 16 Q. -- to see whether or not there
 17 was any neutralization?
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: That is almost an
 21 undoable experiment. That would
 22 require you showing that the serum is
 23 absent of antibodies.
 24 BY MR. KELLER:
 25 Q. That's an undoable experiment?

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1 It's not standard to look at a serum sample, a
 2 negative serum sample that's been -- that has
 3 no antibodies in it to see whether or not --
 4 A. Well, you can have a negative
 5 serum sample, a sample that is negative in the
 6 an assay, but the challenge is how to prove
 7 that that serum is really devoid of an
 8 antibody.
 9 Q. Do you know what a boost
 10 analysis is in a specificity test?
 11 A. No.
 12 Q. You never discussed that with
 13 anybody?
 14 A. Not that I recall.
 15 Q. Nobody recommended doing a boost
 16 analysis specificity test?
 17 A. Not that I recall.
 18 Q. So you never looked at what
 19 would happen if you took blood, virus, and
 20 anti-IgG without mumps antibodies to see
 21 whether or not there would be neutralization
 22 of that virus?
 23 MR. SANGIAMO: Object to the
 24 form.
 25 MR. KELLER: Let me strike that.

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1 BY MR. KELLER:
 2 Q. Did you ever conduct a single
 3 experiment, sir, taking a negative serum
 4 sample that has no antibodies in it, adding
 5 the IgG and adding the virus to see whether or
 6 not there would be neutralization caused by
 7 the anti-IgG?
 8 MR. SANGIAMO: Object to the
 9 form.
 10 THE WITNESS: The prevaccination
 11 sera were included -- were part of the
 12 testing with the anti-IgG but, again,
 13 you can't certify that those sera are
 14 truly devoid of antibody. They could
 15 have maternal antibody. What I don't
 16 recall is how -- if that or how that
 17 neutralization compared with the serum
 18 sample versus a sample -- in each
 19 assay, the serum anti-IgG is present
 20 along with the virus and no antibody.
 21 There are pre-vaccination sera that are
 22 present, some of which are, majority of
 23 which are negative. So, I guess, I'm
 24 having trouble understanding your
 25 compare -- what you're trying to

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1 compare it to.
 2 BY MR. KELLER:
 3 Q. My question is, did you run any
 4 experiments that took negative serum, rabbit
 5 anti-IgG and virus and test that --
 6 MR. SANGIAMO: Objection.
 7 BY MR. KELLER:
 8 Q. -- to see whether or not there
 9 was any neutralization --
 10 MR. SANGIAMO: Object to the
 11 form.
 12 BY MR. KELLER:
 13 Q. -- at any time in your career at
 14 Merck?
 15 MR. SANGIAMO: Object to the
 16 form.
 17 THE WITNESS: Again, what I'm
 18 struggling with is a negative serum.
 19 We had pre-vaccination sera that were
 20 tested.
 21 BY MR. KELLER:
 22 Q. For antibodies?
 23 A. For antibodies, yes.
 24 Q. Explain that to me.
 25 A. The pre-vaccination sera as well

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<p style="text-align: right;">Page 154</p> <p>1 as post-vaccination sera are added to the 2 virus and the anti-IgG in a plaque reduction 3 neutralization assay. And results are 4 calculated as a percentage of plaques relative 5 to a control that didn't have any serum. 6 Q. I understand that. My question 7 is, did you run that assay, that experiment? 8 At any time in your career at Merck, did you 9 ever look and ran an experiment with -- 10 whether it's development of the assay, 11 validation of the assay, or any time before, 12 during or after, in your career at Merck, did 13 you ever run an experiment that took a 14 negative medium sera, negative sera, rabbit 15 anti-IgG and virus to see whether or not there 16 would be a neutralization occurring? 17 MR. SANGIAMO: Object to the 18 form. Asked and answered. 19 THE WITNESS: Again, I'm 20 struggling with the "negative serum" 21 part. 22 BY MR. KELLER: 23 Q. Let me rephrase it. Did you 24 ever -- let me just -- I'll make it more 25 simple.</p>	<p style="text-align: right;">Page 156</p> <p>1 MR. SANGIAMO: This is going in 2 circles. 3 BY MR. KELLER: 4 Q. Let me ask you a question. Was 5 there any analysis of a -- you're saying that 6 there's no serum that you can identify that 7 has negative -- that's negative for 8 antibodies? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: In theory one 12 could -- there could be a potential to 13 show that it was absent of antibodies, 14 but it depends on the assay that you're 15 using. 16 BY MR. KELLER: 17 Q. Is there an industry standard 18 for negative serum? 19 A. I don't -- I'm not aware if 20 there's an industry standard. 21 Q. Can you buy that from other 22 companies, negative sera? 23 A. One could buy negative -- serum 24 that's identified as negative by an assay, 25 whether that's truly negative, an absolute</p>
<p style="text-align: right;">Page 155</p> <p>1 Did you ever run an experiment 2 to count the number of plaques that occurred 3 in a experiment that had negative non-immune 4 serum, rabbit anti-IgG and virus? 5 MR. SANGIAMO: Object to the 6 form. Asked and answered multiple 7 times. And we've been going an hour 8 and a half, but go ahead and answer the 9 question, Doctor. 10 THE WITNESS: Negative or 11 pre-immune sera were tested. 12 BY MR. KELLER: 13 Q. Yes or no, sir. Did you do that 14 analysis? Did you do that, did you ever run 15 that experiment, yes or no? 16 A. Well, the negative serum part is 17 what I'm struggling with because we don't have 18 a serum that's a proven absolute negative. 19 Q. The FDA does, doesn't it? 20 Didn't you actually ask for a sample of that 21 at some point? 22 MR. SANGIAMO: Object to the 23 form. Jeff, take one or two more 24 questions and we're taking a break. 25 THE WITNESS: I don't know.</p>	<p style="text-align: right;">Page 157</p> <p>1 negative I can't say. 2 Q. Can you -- 3 MR. KELLER: I'm not done. 4 MR. SANGIAMO: Well, Jeff, you 5 didn't -- 6 MR. KELLER: Let me finish. I'm 7 not done with this line of questions. 8 MR. SANGIAMO: Well, it's going 9 on forever. So we'll do one more and 10 then we're taking a break. 11 MR. KELLER: If you want to pull 12 your client out of here, you can. 13 BY MR. KELLER: 14 Q. Was there any analysis done with 15 an off-the-shelf negative serum that tested 16 with anti-IgG and without anti-IgG in virus in 17 each sample? Did you ever do that analysis? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: The only samples 21 that I recall testing were pediatric 22 samples where you would have a 23 pre-vaccination, post-vaccination 24 sample. I don't recall that we took an 25 off-the-shelf ever serum that was</p>

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<p>1 identified as negative by some other 2 assay and run that analysis. 3 MR. KELLER: Take a break. 4 VIDEOGRAPHER: The time is now 5 11:55. This ends disc two. 6 - - - 7 (A recess was taken.) 8 - - - 9 VIDEOGRAPHER: The time is now 10 12:11. This begins disc three. You 11 may proceed. 12 BY MR. KELLER: 13 Q. Sir, can I turn your attention 14 to the last page of Exhibit 21 which is 17612. 15 A. Okay. 16 Q. In the first slide there it 17 says, "PLAQUE REDUCTION MUMPS NEUTRALIZATION 18 ASSAY." 19 Do you see that? 20 A. Yes. 21 Q. Do you understand it to be the 22 standard PRN assay that you're familiar with? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: I recognize it to</p>	<p>1 time frame, but it was circulating. 2 Q. That's considered a wild type 3 Tennessee? 4 A. WT indicates wild type. 5 Q. What does wild type mean to you? 6 A. Wild type to me means minimal 7 passage, at least my personal interpretation, 8 minimal passage from a clinical isolate. 9 Q. What do you mean by "a clinical 10 isolate"? 11 A. Clinical isolate meaning a 12 sample that's collected from an infected 13 individual. 14 Q. And do you understand that 15 viruses change over time? 16 MR. SANGIAMO: Object to the 17 form. 18 BY MR. KELLER: 19 Q. Do viruses -- do mumps viruses 20 evolve over time? 21 MR. SANGIAMO: Object to the 22 form. 23 THE WITNESS: There are different 24 genotypes of mumps that have appeared 25 over time. Whether -- so the frequency</p>
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<p>1 be -- the serum dilutions I can't 2 confirm, but a neutralization format 3 that we had run previously in our 4 laboratory. 5 BY MR. KELLER: 6 Q. Is that the Protocol 006 format 7 or methodology? 8 A. There are steps there that are 9 common to mumps plaque assays. I can't say 10 with certainty that is the same one that's 11 used in -- was used in Protocol 006. 12 Q. Did you design this assay that's 13 identified in the first slide? 14 MR. SANGIAMO: Let him finish. 15 THE WITNESS: I don't recall if 16 I did or someone else in the lab did. 17 BY MR. KELLER: 18 Q. The reference there to TN wt 19 mumps, that's Tennessee wild type mumps? 20 A. Yes. 21 Q. And Tennessee wild -- is that a 22 strain of mumps virus that was circulating in 23 the United States in this time frame? 24 A. It was a strain of virus mumps 25 circulating in the US. I don't recall the</p>	<p>1 of which I'm not familiar with. But 2 there are occasions where -- whether 3 it's an evolution or a change, I can't 4 speak to, but there are changes in the 5 virus that have been detected across 6 years. 7 BY MR. KELLER: 8 Q. Is Merck's vaccine strain a wild 9 type under your definition? 10 MR. SANGIAMO: Object to the 11 form. 12 BY MR. KELLER: 13 Q. The virus chain used to make 14 Merck's mumps vaccine, is that -- do you 15 consider that to be a wild type? 16 A. It's the Jeryl Lynn strain. The 17 passage level that it's at is not considered 18 wild type. 19 Q. If I were to get that passage 20 strain, experience that in the wild, I 21 wouldn't get sick? 22 A. That would be the expectation. 23 Q. At what point of passaging do 24 you believe that a kid would likely be 25 infected with the mumps disease if they're</p>

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1 exposed to a Jeryl Lynn with a lower passage?
 2 A. I don't recall the specific
 3 passage level, but I recall that Maurice
 4 Hilleman did a study with what he was calling
 5 an A level and B level of Jeryl Lynn. I don't
 6 recall the passage levels but there was -- the
 7 lower passage level that he evaluated, there
 8 was evidence of parotitis, as best I recall,
 9 in some percentage of the children.
 10 Q. You just don't recall what those
 11 levels were?
 12 A. Offhand I don't remember the
 13 numbers.
 14 Q. You don't recall what passage
 15 level would be considered wild type for Jeryl
 16 Lynn?
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: I have -- so I
 20 don't have a personal opinion on it,
 21 but I recall CBER making a statement of
 22 what passage level they consider to be
 23 wild type.
 24 BY MR. KELLER:
 25 Q. Do you recall what that was?

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1 A. I believe it was 12, as best I
 2 recall.
 3 Q. So anything lower than 12 would
 4 be considered wild type?
 5 A. That was my understanding of
 6 their comment.
 7 Q. Do you recall there being any
 8 discussion in any of the meetings you had
 9 where there was a dispute about whether or not
 10 the Jeryl Lynn strain at any passage should be
 11 used in Protocol 007 PRN assay?
 12 MR. SANGIAMO: Object to the
 13 form.
 14 THE WITNESS: I recall a comment
 15 from Steven Rubin in response to a
 16 publication that he submitted for
 17 review where he made a comment about
 18 the choice of Jeryl Lynn.
 19 BY MR. KELLER:
 20 Q. What was his comment?
 21 A. I don't recall the specifics of
 22 it. My general recollection is that he -- I
 23 don't remember the specific wording of it, but
 24 the understanding I had from it was that he
 25 didn't necessarily agree with Cathy Carbone

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1 and others' position.
 2 Q. That using Jeryl Lynn in
 3 Protocol 007 was proper. Correct?
 4 A. That was his, the view that
 5 he -- that was the implication from the
 6 comment he made, but others at CBER at the
 7 time we were doing Protocol 007 had approved
 8 its low passage virus use.
 9 Q. Was Steven Rubin considered the
 10 preeminent expert on mumps virus testing at
 11 CBER, based on your experience?
 12 A. My -- at the time of our
 13 discussions with the FDA and CBER, at the time
 14 my understanding was that Cathy Carbone was
 15 the expert. I think, as I understand it,
 16 Cathy Carbone has since moved on to either --
 17 I don't know if she's retired, but moved on to
 18 other assignments, and Steve Rubin has been
 19 publishing a lot in the area.
 20 Q. So he's -- you believe he
 21 stepped in to be the CBER expert on mumps
 22 virus now?
 23 MR. SANGIAMO: Objection.
 24 THE WITNESS: Whether he's
 25 CBER's expert, I don't know who else at

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1 CBER who would be contributing.
 2 BY MR. KELLER:
 3 Q. Let me direct your attention
 4 back to Exhibit 21 on 17612. In the third
 5 PowerPoint presentation, in the second bullet
 6 point it says, "A positive mumps neutralization
 7 titer almost certainly ensures protection from
 8 wild type infection."
 9 Do you see that?
 10 A. Yes.
 11 Q. This is based on -- do you
 12 understand that to be based on the PRN assay
 13 identified in this assay?
 14 A. In which -- I'm sorry, in which
 15 assay?
 16 Q. Identified in the first slide.
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: My understanding
 20 is that the assay that we described,
 21 that's described with the Tennessee
 22 mumps, that there was no protection
 23 aspect to that study.
 24 BY MR. KELLER:
 25 Q. So do you understand what --

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<p style="text-align: right;">Page 166</p> <p>1 under this slide it says, "ADVANTAGES TO 2 PARTICIPANTS IN THIS TRIAL FOR SUBJECTS." 3 Do you see that? 4 A. Yes. 5 Q. You understand that they're 6 talking about the assay that's going to be run 7 in this Protocol 007, correct, the purposes 8 behind this protocol? 9 A. I can't say with certainty that 10 they are talking about this particular assay 11 or mumps neutralization in general. 12 Q. Let me ask you more directly. A 13 positive mumps neutralization titer in your 14 assay, the AIGENT, do you believe that ensures 15 protection from wild type infection? 16 A. I have no experience in that 17 area. I don't have any direct experience 18 with -- 19 Q. Were you ever -- go ahead. 20 A. -- with clinical relevance. 21 Q. Were you ever -- did you ever 22 discuss the development of Protocol 007 with 23 anybody at Merck? 24 A. I'm sorry? 25 Q. Strike that. That's a bad</p>	<p style="text-align: right;">Page 168</p> <p>1 form. 2 THE WITNESS: That's what it 3 says. 4 BY MR. KELLER: 5 Q. In that greater than 1 to 4, 6 that -- is that the same serostatus cutoff 7 that was used in your PRN -- 8 MR. SANGIAMO: Object to the 9 form. 10 BY MR. KELLER: 11 Q. -- for definition of seroconverter? 12 A. I don't recall what dilutions we 13 used. 14 MR. KELLER: Fair enough. Let 15 me mark this next exhibit as Exhibit 22. 16 - - - 17 (Exhibit Krah-22, PowerPoint 18 presentation, 17647 - 17762, was marked 19 for identification.) 20 - - - 21 BY MR. KELLER: 22 Q. For the record, Exhibit 22 is 23 also part of the same packet, the file 24 regarding the March 15 and 16, 1999, 25 investigator meeting relating to the mumps</p>
<p style="text-align: right;">Page 167</p> <p>1 question. 2 Did you ever discuss the 3 clinical relevance of the assay you were 4 developing for Protocol 007 with anybody at 5 Merck? 6 A. Not that I recall. 7 Q. In the second bullet point, the 8 second slide it says primary -- sorry, strike 9 that. 10 In the second slide of this 11 investigator meeting presentation it says, 12 "PRELIMINARY GUIDELINES FOR THE PRN ASSAY." 13 Do you see that? 14 A. Yes. 15 Q. It says, Negative (not 16 protected) less than 1 to 2. 17 Do you have an understanding of 18 what's meant by that? 19 A. The only understanding I have is 20 what the words say, that if the titer is less 21 than 1 to 2, it's considered negative and I'll 22 say assume not protected. 23 Q. So in a sample that's greater 24 than equal 1 to 4 is protected. Correct? 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 169</p> <p>1 expiry study. And it bears Bates stamp number 2 17647 through 17762. 3 Sir, I'll ask you if you recall 4 seeing -- there's two documents in this 5 packet. One is a PowerPoint presentation and 6 then the second one starting at 17654 is a 7 Protocol 007-00 product V205C. I'll ask you, 8 if you recall, seeing either of these two 9 documents before today? 10 A. They don't look familiar to me. 11 Q. Do you recall -- again, you 12 don't recall participating in this 13 presentation or seeing any of the 14 presentations that were given to it. Correct? 15 MR. SANGIAMO: Object to the 16 form. 17 THE WITNESS: All I can say is 18 they don't look familiar to me. 19 BY MR. KELLER: 20 Q. Again, you don't have any reason 21 to believe you didn't see them, you just don't 22 recall seeing them. Correct? 23 A. If this was -- if this is the 24 same meeting or is this the same meeting from 25 Texas?</p>

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<p style="text-align: right;">Page 170</p> <p>1 Q. Yes.</p> <p>2 MR. SANGIAMO: You don't have to</p> <p>3 accept that representation, but he's</p> <p>4 premising his question on the</p> <p>5 supposition that it is. It's possible.</p> <p>6 THE WITNESS: If it was that</p> <p>7 meeting and that meeting said I was an</p> <p>8 attendee, then I would have been there,</p> <p>9 but I don't have a recollection of</p> <p>10 seeing -- I don't recall seeing these</p> <p>11 or have a memory of them.</p> <p>12 BY MR. KELLER:</p> <p>13 Q. That's fine. Let me direct your</p> <p>14 attention, then, to 17654, the protocol. Take</p> <p>15 whatever time you want to look at this</p> <p>16 protocol, it's very long. We can go off the</p> <p>17 record if you want to read it cover to cover</p> <p>18 because I may have some questions for you on</p> <p>19 it.</p> <p>20 Do you recall ever seeing the</p> <p>21 protocol for Protocol 007?</p> <p>22 A. I don't remember.</p> <p>23 Q. And so do you recall -- let me</p> <p>24 direct your attention to -- have you ever seen</p> <p>25 a protocol before?</p>	<p style="text-align: right;">Page 172</p> <p>1 time you want to to look at this</p> <p>2 protocol.</p> <p>3 MR. SANGIAMO: No, I don't</p> <p>4 agreed that you get to soak up his day</p> <p>5 by handing him really long documents</p> <p>6 and then having it be off the record.</p> <p>7 So let's just see if we can avoid a</p> <p>8 fight, see if it works. And if there</p> <p>9 might just be sections that he can read</p> <p>10 depending on what your questions are,</p> <p>11 that might solve the problem.</p> <p>12 MR. KELLER: This is the</p> <p>13 protocol for Protocol 007, and the fact</p> <p>14 that he says he doesn't recall ever</p> <p>15 seeing it again, you want him to spend</p> <p>16 the next 30 minutes on the record</p> <p>17 reviewing it the first time to answer</p> <p>18 questions about it, I don't think</p> <p>19 that's fair, and we would likely go</p> <p>20 back to the court for more time if</p> <p>21 that's the position you want to take.</p> <p>22 Because there are a lot of documents</p> <p>23 and unfortunately some of these</p> <p>24 documents are longer and we have</p> <p>25 limited time with him. If you are</p>
<p style="text-align: right;">Page 171</p> <p>1 A. I've seen sections of protocols.</p> <p>2 It doesn't mean I read it and understood it,</p> <p>3 but I remember seeing documents that were part</p> <p>4 of protocols before. I don't remember how</p> <p>5 much I understood it.</p> <p>6 Q. Fair enough. Let's look at a</p> <p>7 couple pages here and see if that refreshes</p> <p>8 your memory if you've seen parts of this</p> <p>9 protocol as part of your job developing and</p> <p>10 running the experiments for Protocol 007's</p> <p>11 AIGENT assay.</p> <p>12 MR. SANGIAMO: What I propose we</p> <p>13 do here, if you're going to --</p> <p>14 MR. KELLER: Why don't we go off</p> <p>15 the record.</p> <p>16 MR. SANGIAMO: Why don't you</p> <p>17 start your questions, if you're just</p> <p>18 asking if he's seen certain things,</p> <p>19 then that's fine. If you're going to</p> <p>20 start getting into asking him to</p> <p>21 interpret the language, that might</p> <p>22 require a different level of his</p> <p>23 review. So why don't you just --</p> <p>24 MR. KELLER: Why don't we just</p> <p>25 go off the record and take whatever</p>	<p style="text-align: right;">Page 173</p> <p>1 going to require us to take that time</p> <p>2 for him to review a document on the</p> <p>3 record, then we're going to go back and</p> <p>4 seek additional time with this court.</p> <p>5 You decide.</p> <p>6 MR. SANGIAMO: I suggest we see</p> <p>7 where it goes.</p> <p>8 MR. KELLER: Sure.</p> <p>9 MR. SANGIAMO: Start your</p> <p>10 questions, if it looks like he needs to</p> <p>11 read, he will read as much of it as he</p> <p>12 needs to read and maybe we won't have</p> <p>13 any kind of problem.</p> <p>14 MR. KELLER: Sure.</p> <p>15 BY MR. KELLER:</p> <p>16 Q. Let me direct your attention,</p> <p>17 you've -- sir, you've reviewed protocols in</p> <p>18 the past. Are you familiar with the format of</p> <p>19 them?</p> <p>20 A. I wouldn't say reviewed. I have</p> <p>21 seen them. I wouldn't call it a -- I wouldn't</p> <p>22 constitute -- qualify it as a review.</p> <p>23 Q. Let's turn to your attention to</p> <p>24 the table of contents on 17655. It's broken</p> <p>25 up into a couple of different sections. I is</p>

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1 "CLINICAL SECTIONS," "ADMINISTRATIVE AND
2 REGULATORY SECTIONS." Do you see that? And
3 "SIGNATURES." Do you see that on 17655 and --
4 A. The second one I don't.
5 Q. On 17657. Roman numeral I,
6 Roman numeral II, Roman numeral III. Do you
7 see that?
8 A. Yes.
9 Q. On the "CLINICAL SECTIONS" under
10 III [sic] it says, "OBJECTIVES." Do you see
11 that on 17655?
12 MR. SANGIAMO: Number III?
13 BY MR. KELLER:
14 Q. Roman numeral I(C), "OBJECTIVES."
15 Do you see that?
16 A. Yes.
17 Q. Do you understand what
18 objectives are in a protocol?
19 A. No.
20 Q. Let me direct your attention to
21 17665 -- strike that.
22 Let me direct your attention to
23 17693 under F, "EFFICACY/PHARMACOKINETICS
24 /IMMUNOGENICITY, ETC., MEASUREMENTS." In the
25 second paragraph it says, "Serologic testing

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1 will be performed by Merck Research
2 Laboratories..., West Point, PA."
3 Do you see that?
4 A. Yes.
5 Q. What do you understand serologic
6 testing to mean generally outside of this
7 protocol?
8 A. It could be a variety of things.
9 It would depend on what this -- the document
10 indicates is the specific assay.
11 Q. Let me ask you, for Protocol
12 007, did you do serologic testing in your lab?
13 A. Yes.
14 Q. And what serologic testing did
15 you do?
16 A. For Protocol 007?
17 Q. Yes.
18 A. The mumps AIGENT assay.
19 Q. So you ran the kid's serum in
20 that assay. Correct?
21 A. Yes.
22 Q. Let me direct your attention to
23 17706, under "DATA ANALYSIS." In the first
24 sentence it says -- let me know when you're
25 there. The first sentence says, On the

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1 subjects enrolled in each of the treatment
2 groups, 5 percent are expected to be initially
3 seropositive.
4 Do you see that? The first
5 sentence.
6 A. Yes.
7 Q. The treatment groups, did you
8 understand that to be the three doses that
9 were run in the AIGENT?
10 MR. SANGIAMO: Object to the --
11 you said did he understand?
12 MR. KELLER: Yes.
13 MR. SANGIAMO: Object to the
14 form.
15 THE WITNESS: I don't recall
16 that specific part of the document,
17 seeing that before in this document.
18 BY MR. KELLER:
19 Q. Did you ever learn that there is
20 an expectation that only -- what do you
21 understand initially seropositive to mean in a
22 plaque reduction neutralization assay?
23 A. My general understanding of that
24 would be that the pre-vaccination, 5 percent
25 of the pre-vaccination sera would be expected

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1 to be positive.
2 Q. What does that mean to you, what
3 does seropositive mean?
4 A. It means that there's a positive
5 neutral -- the serum is neutralizing in the --
6 it's giving a positive neutralization result.
7 Q. For mumps specific antibodies?
8 A. Yes.
9 Q. So is it the understanding that
10 those kids are immune from the disease because
11 they've already got mumps neutralizing
12 antibodies in their bloodstream?
13 MR. SANGIAMO: Object to the
14 form.
15 THE WITNESS: I don't know that
16 -- the clinical conclusion from that
17 result.
18 BY MR. KELLER:
19 Q. You don't. This expectation of
20 5 percent being pre-positive, have you ever
21 heard that expectation before?
22 A. I've heard of estimates of
23 initially seropositive. I can't say that the
24 5 percent is familiar.
25 Q. Have you done any research to

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<p style="text-align: right;">Page 178</p> <p>1 determine what would be expected for kids to 2 be immune from mumps prior to being vaccinated? 3 A. Personally, no. 4 MR. SANGIAMO: Object to the 5 form. 6 BY MR. KELLER: 7 Q. Has anybody, are you aware of 8 anybody -- strike that. 9 Are you aware of anybody 10 connected with Protocol 007 doing any research 11 to determine what the expectation was for kids 12 before they're vaccinated to be immune from 13 mumps disease? 14 MR. SANGIAMO: Object to the 15 form. 16 THE WITNESS: I'm not aware, I'm 17 not familiar with whether such studies 18 were done. 19 BY MR. KELLER: 20 Q. You made projections for 21 pre-positive rates, didn't you, when you ran 22 the AIGENT? 23 A. There were estimates of the 24 expected pre-positive rates based on the 25 results of our development studies.</p>	<p style="text-align: right;">Page 180</p> <p>1 pre-positive results were for the ELISA 2 testing? 3 A. No. 4 MR. SANGIAMO: Object to the 5 form. 6 BY MR. KELLER: 7 Q. Nobody ever told you? 8 MR. SANGIAMO: Object to the 9 form. 10 THE WITNESS: I don't recall. 11 BY MR. KELLER: 12 Q. Would that have been relevant 13 for you to understand a kid identified as 14 having no mumps antibodies in an ELISA, to use 15 that as a comparison to what was being seen in 16 the AIGENT? 17 MR. SANGIAMO: Object to the 18 form. 19 THE WITNESS: I'm sorry, that 20 doesn't make sense. 21 BY MR. KELLER: 22 Q. It doesn't make sense to you? 23 An ELISA identifies mumps antibodies. 24 Correct? Isn't that the whole purpose of an 25 ELISA, a mumps ELISA assay, to identify mumps</p>
<p style="text-align: right;">Page 179</p> <p>1 Q. Other than running your 2 development studies to get a pre-positive 3 rate, are you aware of any other control to 4 identify whether or not these kids are, in 5 fact, immune from disease, from mumps? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: I'm not aware of 9 other -- are you asking if there is 10 another independent test of antibody in 11 those sera? 12 BY MR. KELLER: 13 Q. Did you do any other independent 14 testing to determine seropositive rates for 15 kids that would expect in this study of the 16 this nature PRN study? 17 MR. SANGIAMO: Object to the 18 form. 19 THE WITNESS: I didn't 20 personally do it. 21 BY MR. KELLER: 22 Q. Did you ever compare it against 23 ELISA results for pre-positivity? 24 A. I did not. 25 Q. Are you aware of what the</p>	<p style="text-align: right;">Page 181</p> <p>1 antibodies? 2 A. Yes. 3 Q. So if a kid is pre-positive for 4 an ELISA mumps antibody test, that would 5 presume that the kid has mumps antibodies. 6 Correct? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: It would indicate 10 that that serum has detectible 11 antibodies. 12 BY MR. KELLER: 13 Q. You don't think that information 14 to be at all relevant in determining the 15 pre-positive rate for your plaque reduction 16 neutralization assay? 17 A. From my view, no. 18 Q. Why? 19 A. They're independent assays. I 20 wouldn't -- at least in other assays that are 21 -- other neutralization assays I've run, I'm 22 not aware of any suggestion of -- a suggestion 23 of using the ELISA as a guide for what to 24 expect in that assay. 25 Q. Have you ever -- are you aware</p>

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<p style="text-align: right;">Page 182</p> <p>1 of anybody who has correlated an ELISA assay</p> <p>2 to a plaque reduction neutralization assay for</p> <p>3 mumps?</p> <p>4 A. Yes.</p> <p>5 Q. Who?</p> <p>6 A. Steve Rubin is one of them, one</p> <p>7 person.</p> <p>8 Q. For determining whether or not</p> <p>9 the assay is -- when did that happen?</p> <p>10 A. I don't recall specific years,</p> <p>11 but he's published on those studies.</p> <p>12 Q. Has there been a correlation</p> <p>13 between an ELISA assay and protection from</p> <p>14 disease?</p> <p>15 MR. SANGIAMO: Object to the</p> <p>16 form.</p> <p>17 THE WITNESS: From my</p> <p>18 understanding, there is no correlate of</p> <p>19 protection from -- protection from</p> <p>20 disease for mumps.</p> <p>21 BY MR. KELLER:</p> <p>22 Q. Do you understand what the term</p> <p>23 "efficacy" means?</p> <p>24 A. I have a general understanding</p> <p>25 of that.</p>	<p style="text-align: right;">Page 184</p> <p>1 protection in the broader population.</p> <p>2 Q. Do you recall ever representing</p> <p>3 in a document that the assay that you ran is</p> <p>4 linked to efficacy?</p> <p>5 A. Not that I recall.</p> <p>6 Q. Would that surprise you if you</p> <p>7 saw a document linked to your name, that you</p> <p>8 represented that this assay, the assay that</p> <p>9 you ran was linked to efficacy?</p> <p>10 MR. SANGIAMO: Object to the</p> <p>11 form.</p> <p>12 THE WITNESS: I don't recall.</p> <p>13 I'm not aware of one study that I might</p> <p>14 link to.</p> <p>15 BY MR. KELLER:</p> <p>16 Q. Would that surprise you if</p> <p>17 somebody represented that the assay that you</p> <p>18 developed, the AIGENT, was linked --</p> <p>19 represented as being linked to efficacy?</p> <p>20 MR. SANGIAMO: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: Well, the</p> <p>23 statement of the link to efficacy would</p> <p>24 be a statement that would be beyond my</p> <p>25 expertise, require clinical and</p>
<p style="text-align: right;">Page 183</p> <p>1 Q. What's your understanding?</p> <p>2 A. That that's the -- in a</p> <p>3 controlled clinical setting, the protection</p> <p>4 from -- the protection from disease achieved</p> <p>5 during a controlled clinical study.</p> <p>6 Q. Did your -- the AIGENT you</p> <p>7 developed, did that show efficacy?</p> <p>8 MR. SANGIAMO: Object to the</p> <p>9 form.</p> <p>10 THE WITNESS: There -- my</p> <p>11 understanding, there was no protection</p> <p>12 in the study. This was an</p> <p>13 immunogenicity study. So efficacy,</p> <p>14 from my understanding, would require</p> <p>15 evaluating protection from disease in</p> <p>16 the vaccinees.</p> <p>17 BY MR. KELLER:</p> <p>18 Q. Did you ever -- do you know what</p> <p>19 effectiveness means?</p> <p>20 A. I have a general understanding</p> <p>21 of that.</p> <p>22 Q. What's your understanding, sir?</p> <p>23 A. My general understanding of that</p> <p>24 is protection from disease in a global world</p> <p>25 setting versus a controlled clinical setting</p>	<p style="text-align: right;">Page 185</p> <p>1 regulatory input. So if a document did</p> <p>2 exist, my input would not have been</p> <p>3 beyond the assay description.</p> <p>4 BY MR. KELLER:</p> <p>5 Q. When you were developing the</p> <p>6 AIGENT that ultimately got used in Protocol</p> <p>7 007 -- strike that.</p> <p>8 Let me direct your attention</p> <p>9 back to Exhibit 22, in particular at 17720,</p> <p>10 under "COMPLIANCE WITH LAW, AUDIT, AND</p> <p>11 DEPARTMENT."</p> <p>12 You testified that you may have</p> <p>13 seen pieces of protocols. Do you ever recall</p> <p>14 seeing pieces of protocols that discussed how</p> <p>15 the clinical studies would be conducted?</p> <p>16 A. I do not.</p> <p>17 Q. In this protocol for Protocol</p> <p>18 007, it's dated February 2, 1999. Do you see</p> <p>19 that in the bottom right-hand corner?</p> <p>20 A. Yes.</p> <p>21 Q. You were working on that -- on</p> <p>22 Protocol 007 at this time frame, weren't you?</p> <p>23 A. I don't recall the date.</p> <p>24 Q. You don't recall. Here it says,</p> <p>25 "COMPLIANCE WITH LAW, AUDIT, AND DEPARTMENT,"</p>

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<p style="text-align: right;">Page 186</p> <p>1 the first paragraph, can you read the first 2 sentence on 17720? 3 A. The first, "By signing this 4 protocol...", that one? 5 Q. Yes. 6 A. "By signing this protocol, the 7 investigator agrees to conduct the study in an 8 efficient and diligent manner and in 9 conformance with this protocol; generally 10 accepted standards of Good Clinical Practice; 11 and all applicable federal, state, and local 12 laws, rules and regulations relating to the 13 conduct of the clinical study." 14 Q. It's your testimony that you 15 didn't have an understanding that the samples 16 that you ran for Protocol 007 would be 17 required to be run under the Good Clinical 18 Practices because you didn't even know what 19 that was, did you? 20 A. I was not familiar with what 21 that term referred to nor that we were -- that 22 it applying to the testing laboratory. 23 MR. SANGIAMO: Jeff, if you're 24 going to ask him questions about the 25 substance, why don't you just go ahead</p>	<p style="text-align: right;">Page 188</p> <p>1 you understand what quality control and 2 quality assurance is? 3 A. I've heard the terms before. 4 How it applies in this particular case I am 5 not familiar with. 6 Q. Is it a department at Merck that 7 handles quality control and quality assurance? 8 A. There are people at Merck whose 9 job includes that. I don't recall whether 10 there is a specific department that covers 11 those particular items alone or if they 12 include other responsibilities. 13 Q. Do you recall -- do you 14 understand what the difference is between 15 quality control and quality assurance? 16 A. Not offhand. 17 Q. Here it says, "By signing this 18 protocol, the SPONSOR agrees to be responsible 19 for implementing and maintaining quality 20 control and quality assurance systems with 21 written SOPs to ensure that trials are 22 conducted and data generated, documented, and 23 reported in compliance with the protocol, 24 accepted standards of Good Clinical Practice, 25 and all applicable federal, state, and local</p>
<p style="text-align: right;">Page 187</p> <p>1 and read that very short section. 2 BY MR. KELLER: 3 Q. Sure. Why don't you read this 4 section, it's only three pages, take your 5 time. 6 A. Okay. 7 MR. SANGIAMO: Also read the 8 final paragraph. 9 BY MR. KELLER: 10 Q. Just those two pages. 11 A. Okay. 12 Q. Having read these three 13 sections, does that refresh your memory 14 whether or not you've seen this language in 15 Protocol 007? 16 MR. SANGIAMO: I'm sorry, the 17 which three section? I thought he read 18 two sections. 19 MR. KELLER: Section H and I. 20 BY MR. KELLER: 21 Q. Those two pages. 22 A. That does not change my -- I 23 don't recall. 24 Q. So in the section I under 25 "QUALITY CONTROL AND QUALITY ASSURANCE," do</p>	<p style="text-align: right;">Page 189</p> <p>1 laws, rules and regulations relating to the 2 conduct of the clinical study." 3 Do you see that? 4 A. Yes. 5 Q. That's reference to Protocol 6 007. Correct? Is that a fair statement, the 7 clinical study referenced there is Protocol 8 007? 9 A. That's what it appears to be, 10 yes. 11 Q. Did you understand -- and you 12 ran the serum for Protocol 007, correct, in 13 your lab? 14 A. Yes. 15 Q. Does that lead you to believe 16 that your lab should have been complying with 17 the accepted standard for Good Clinical 18 Practices? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: I don't have 22 experience whether that -- the 23 description as written here applies to 24 the testing laboratory. 25 BY MR. KELLER:</p>

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<p style="text-align: right;">Page 190</p> <p>1 Q. The reference here to sponsor, 2 that's Merck, right? Merck was the sponsor 3 for this protocol? 4 A. That's my -- I can't say for 5 certain, but that's my understanding of the 6 wording. 7 Q. During the time that you ran the 8 samples for Protocol 007, were there any SOPs 9 in place for quality control that related to 10 those clinical samples? 11 A. I don't recall. 12 Q. Were there any quality assurance 13 SOPs that were in place with respect to the 14 running of the clinical samples in Protocol 15 007 that you recall? 16 A. I don't recall. 17 MR. KELLER: Let me mark this 18 next exhibit as Exhibit 23. 19 - - - 20 (Exhibit Krah-23, E-mail string, 21 337141 - 337157 & 121082, was marked 22 for identification.) 23 - - - 24 BY MR. KELLER: 25 Q. For the record, Exhibit 23 is a</p>	<p style="text-align: right;">Page 192</p> <p>1 who is Mande Lyon? 2 A. I don't recall. 3 Q. The subject here is "MMR II 4 Protocol 007 IDSA Poster Draft." 5 Do you see that? 6 A. Yes. 7 Q. What's the IDSA? 8 A. It's, as best I recall, an 9 organization. I don't recall what it stands 10 for. 11 Q. Do you recall ever giving a 12 presentation at that organization regarding 13 Protocol 007? 14 A. Clarification, me personally 15 or -- 16 Q. You personally. 17 A. I don't recall personally giving 18 a presentation. 19 Q. Do you recall, has anybody ever 20 presented on the results of Protocol 007 to 21 anybody outside of Merck other than the FDA or 22 CBER? 23 MR. SANGIAMO: Answer if you 24 know obviously. 25 THE WITNESS: I don't know.</p>
<p style="text-align: right;">Page 191</p> <p>1 document that bears Bates stamp number 337141 2 through 157. And there's a separate document 3 attached to this that bears Bates number 4 121082. I'll keep these together as Exhibit 23. 5 Sir, can you tell me if you 6 recognize the attachments? The attachment 7 says "Study of MMR II at Mumps Expiry 8 Potency," and, sir, you're identified as one 9 of the writers of this document. And the last 10 page at 121082 is actually a poster. Correct? 11 MR. SANGIAMO: Hang on a second. 12 What's the question? 13 MR. KELLER: I'll start again. 14 BY MR. KELLER: 15 Q. Sir, if you look on the first 16 page, 337141, there's an e-mail from a Mande 17 Lyon to you. Do you see that, August 17, 18 2004? 19 A. August -- I'm sorry. The 20 initial one, the August 17, 2004, yes. 21 Q. Typically the way e-mails work 22 when they're printed up is they start with -- 23 A. The more recent. 24 Q. Yeah. So the top of it is the 25 more recent. The bottom is later in time. So</p>	<p style="text-align: right;">Page 193</p> <p>1 This document suggested that this 2 was -- is the planned presentation, but 3 I don't know what's presented. 4 BY MR. KELLER: 5 Q. Did you ever publish your 6 findings in Protocol 007? Let me strike that. 7 Did you ever prepare a paper for 8 publication from your findings in Protocol 9 007? 10 A. Did I or did Merck? 11 Q. Were you involved in that? 12 A. I was -- yes, there was a 13 publication put together in which I was a 14 co-author. 15 Q. Was that ever published? 16 A. Not to my knowledge. 17 Q. Do you know why? 18 MR. SANGIAMO: Dr. Krah, you 19 should exclude from any answer anything 20 that involves communications from 21 counsel. So do you know of reasons 22 other than anything that would have 23 been communicated to you by counsel? 24 THE WITNESS: No. 25 BY MR. KELLER:</p>

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1 Q. This is a 2004 poster. Correct?
 2 A. The date is from 2004. I don't
 3 know when the actual --
 4 Q. Did you draft --
 5 MR. SANGIAMO: You don't know
 6 when the actual what?
 7 THE WITNESS: Presentation was.
 8 BY MR. KELLER:
 9 Q. Did you draft this?
 10 A. That is not typical -- no, I did
 11 not draft it.
 12 Q. Your name is on it, though.
 13 Correct?
 14 A. Yes.
 15 Q. So who would typically draft
 16 these types of documents at Merck?
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: It varies. I was
 20 looking -- typically the first author
 21 is the one who prepared it. But the
 22 first author is not a -- doesn't look
 23 like is a Merck person. So I can't say
 24 with certainty who was the lead in
 25 drafting it.

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1 BY MR. KELLER:
 2 Q. Mande Lyon is from Merck,
 3 according to this poster. Do you see that?
 4 A. Yes.
 5 Q. You don't know who that is?
 6 A. Other than like on the page
 7 before it says she's associate medical program
 8 clinical specialist, I know her, the name is
 9 familiar to me, but I don't have any other
 10 specific recollection.
 11 Q. If you didn't draft it, why is
 12 your name on it?
 13 MR. SANGIAMO: Objection.
 14 Answer if you know.
 15 THE WITNESS: I can't say with
 16 certainty. There's a general
 17 scientific rationale for it, but I
 18 can't say with certainty for this
 19 particular one why I'm on it.
 20 BY MR. KELLER:
 21 Q. Do you recall commenting on this
 22 draft?
 23 A. The e-mail indicates that I had
 24 some comments to the poster, so yes.
 25 Q. So you reviewed it?

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1 A. This suggests, yeah, the e-mail
 2 suggests that I reviewed it.
 3 Q. When you reviewed it, did you
 4 see anything that was incorrectly stated in
 5 this poster?
 6 A. Not that I was aware of.
 7 Q. And if there was something
 8 incorrect here, would you have -- you would
 9 have raised that, wouldn't you have?
 10 MR. SANGIAMO: Dr. Krah, why
 11 don't you take a look at the document
 12 since he's asking the substance of it.
 13 BY MR. KELLER:
 14 Q. I'm asking generally without
 15 looking at the document. If there was
 16 something incorrect in a poster like this, you
 17 would have raised that objection, wouldn't you
 18 have?
 19 MR. SANGIAMO: You said a poster
 20 like this. So that means he needs to
 21 look at the document to find out what
 22 the document is about.
 23 BY MR. KELLER:
 24 Q. You can't answer that question
 25 without looking at the document?

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1 MR. SANGIAMO: What's your
 2 question? Rephrase your question.
 3 BY MR. KELLER:
 4 Q. If you would have seen a
 5 statement that was incorrect in a poster that
 6 was being published with your name on it, sir,
 7 would you have raised that objection before it
 8 was published?
 9 A. If I was aware of a mistake, I
 10 would have raised it.
 11 Q. Fair enough. Take a second to
 12 look at this poster and tell me -- it's
 13 multiple pages. I really only have one
 14 question. Actually two questions.
 15 On page 337144 --
 16 MR. SANGIAMO: He's still
 17 looking at the document, Jeff.
 18 THE WITNESS: Okay.
 19 BY MR. KELLER:
 20 Q. Do you see anything incorrectly
 21 stated in this poster?
 22 A. In my review, my focus would be
 23 limited to my experience with the
 24 neutralization assay. So I did not see
 25 anything that was incorrect regarding those --

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1 the neutralization assay details.
 2 Q. The numbers?
 3 A. Either the numbers or the format
 4 of the assay.
 5 Q. So under this poster that has
 6 your name on it, sir, it says, "Study
 7 Rationale." Do you see that on the first page
 8 of it?
 9 A. Okay.
 10 Q. What do you understand the study
 11 rationale to mean?
 12 A. All I can say literally what the
 13 words are written here. I don't have any
 14 understanding beyond that.
 15 Q. Your name is on this thing so
 16 why don't you tell me what your understanding
 17 is?
 18 MR. SANGIAMO: He just answered
 19 your question, Jeff.
 20 BY MR. KELLER:
 21 Q. Tell me what you understand it
 22 to be.
 23 A. Literally what the words say
 24 here.
 25 Q. Is it the rationale for Protocol

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1 007? Is that a fair assessment?
 2 A. If there is --
 3 Q. Look at the -- on the next page,
 4 on the third bullet point from the bottom, do
 5 you see that? It says, "To determine the
 6 minimum mumps virus potency at expiry in
 7 MMR II, a clinical trial was conducted among
 8 children 12 to 18 months of age"
 9 Do you see that?
 10 A. Yes.
 11 Q. That's talking about the AIGENT
 12 that you ran. Correct? That's the clinical
 13 trial?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: There was an
 17 antibody assay that was part of the
 18 clinical trial. The clinical trial
 19 also included the actual preparation,
 20 administration of the vaccine.
 21 BY MR. KELLER:
 22 Q. Fair enough. In the next bullet
 23 point says -- can you read the next bullet
 24 point for the record, please?
 25 A. "Antibody response measured by

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1 mumps-virus specific plaque reduction
 2 neutralization (PRN) assay was used as a
 3 surrogate of vaccine efficacy; ELISA assays
 4 for mumps antibodies were also performed."
 5 Q. So the statement here that the
 6 mumps virus specific plaque reduction
 7 neutralization (PRN) assay was used as a
 8 surrogate for vaccine efficacy, that was
 9 Protocol 007, wasn't it?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 BY MR. KELLER:
 13 Q. The AIGENT that you worked on?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: The Protocol
 17 007 -- the AIGENT assay was used in
 18 Protocol 007.
 19 BY MR. KELLER:
 20 Q. Correct. So what they're
 21 referencing here, was there any other mumps
 22 virus specific plaque reduction neutralization
 23 assays as part of Protocol 007 other than the
 24 AIGENT?
 25 A. Not that I'm aware of.

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1 Q. Here it represents that that
 2 assay was used as a surrogate of vaccine
 3 efficacy. Do you see that?
 4 A. Yes.
 5 Q. Is that the first time you've
 6 ever seen that your -- the analysis that you
 7 ran, the studies that you ran, the results
 8 that you ran were going to be used as a
 9 surrogate of vaccine efficacy?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: I can't say with
 13 certainty it's the first I saw it, but
 14 I don't recall seeing that.
 15 BY MR. KELLER:
 16 Q. What do you understand that to
 17 mean, a surrogate of vaccine efficacy?
 18 A. That's an area beyond my
 19 expertise.
 20 Q. You don't understand after
 21 working in research, vaccine research since
 22 1988 what a surrogate of vaccine efficacy
 23 means?
 24 A. That's correct.
 25 MR. SANGIAMO: Jeff, we've been

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1 going about 45 minutes.
 2 MR. KELLER: Let's go for lunch.
 3 VIDEOGRAPHER: The time is now
 4 12:57. This concludes disc three.
 5 - - -
 6 (A recess was taken.)
 7 - - -
 8 VIDEOGRAPHER: The time is now
 9 2:08. This begins disc four. You may
 10 proceed.
 11 MR. KELLER: I'm going to mark
 12 as Exhibit 24 a document that bears
 13 Bates-stamped number 625837 through
 14 839, and it's an e-mail, and there's an
 15 attached document to the e-mail.
 16 - - -
 17 (Exhibit KraH-24, 10/6/98 E-mail
 18 with attachment, 625837 - 625839, was
 19 marked for identification.)
 20 - - -
 21 BY MR. KELLER:
 22 Q. In the e-mail dated at the top
 23 of the page October 6, 1998, from Henrietta
 24 Ukwu to a series of individuals, and, sir, you
 25 are one of the cc's on this e-mail entitled:

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1 Mumps expiry; summary of prep meeting on
 2 September 30 for CBER telecon.
 3 Do you see that?
 4 A. Yes.
 5 Q. Do you recall receiving this
 6 e-mail?
 7 MR. SANGIAMO: Obviously take a
 8 minute to look at it, Dr. KraH, read it
 9 to your satisfaction.
 10 THE WITNESS: I don't have a
 11 recollection. I see my name on the cc
 12 list, but I don't recall -- it doesn't
 13 provide a memory.
 14 BY MR. KELLER:
 15 Q. Do you have any reason to
 16 believe you didn't receive it?
 17 A. If I'm on the cc list, it would
 18 imply that it was sent to me. So I don't have
 19 any reason to believe it was not sent to me.
 20 Q. Was it your practice to review
 21 e-mails that you received?
 22 A. My practice, as best I recall,
 23 was to read the -- or look at who it's from
 24 and read the subject, the subject line. I
 25 can't say that every -- I can't say I then

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1 read the content of everything.
 2 Q. So it's fair to say if somebody
 3 of importance e-mailed you something, you
 4 would read that e-mail. Correct?
 5 MR. SANGIAMO: Object to the
 6 form.
 7 THE WITNESS: I would say it
 8 would -- perhaps it would depend on the
 9 subject and who the person was. A
 10 person of importance would be relative
 11 to me. It may be an important person
 12 in the organization but not necessarily
 13 in my reporting structure.
 14 BY MR. KELLER:
 15 Q. Gotcha. Who is Henrietta Ukwu?
 16 A. I don't recall her title. I'd
 17 be guessing at what her -- even what group she
 18 was in.
 19 Q. She was senior management at
 20 Merck, wasn't she, at this time frame?
 21 A. I don't know -- I don't know
 22 what constitutes -- well, I don't recall her
 23 position and title and whether that
 24 constituted senior management or not.
 25 Q. And here under subject, it says,

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1 Mumps expiry; summary of prep meeting 600 for
 2 CBER telecon. Would that have been of
 3 interest to you during this time frame?
 4 A. I don't -- I don't -- it's not
 5 obvious to me that it would have been of
 6 interest, but I -- so I can't say one way or
 7 the other whether it would be of interest.
 8 Q. In the first sentence it says,
 9 "Please note the summary, from Dr. Chirgwin..."
 10 Who is Dr. Chirgwin?
 11 A. The Dr. Chirgwin I know is Keith
 12 Chirgwin. I don't know his position at the
 13 time.
 14 Q. Do you recall, is he -- do you
 15 recall when he left Merck?
 16 A. No.
 17 Q. Do you recall him working in
 18 regulatory affairs?
 19 A. I recall him working, as best I
 20 can recall, in regulatory affairs at some
 21 point in his career at Merck.
 22 Q. Do you recall him reporting to
 23 Henrietta Ukwu in regulatory affairs?
 24 A. That, I don't recall.
 25 Q. This topic of mumps expiry, you

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1 don't recall if you were working on the
 2 development of the PRN assay during this time
 3 frame?
 4 A. I don't recall.
 5 Q. Let me direct your attention to
 6 the last sentence. It says, "The key members
 7 of the team are copied on this memo...."
 8 Do you see that?
 9 A. Yes.
 10 Q. And under the cc, you understand
 11 that's carbon copy. Correct?
 12 MR. SANGIAMO: Object to the
 13 form.
 14 BY MR. KELLER:
 15 Q. Do you understand what copy
 16 means?
 17 A. cc -- yeah, cc just means it's
 18 someone who is copied, whether it's -- in the
 19 olden days my understanding was carbon copy.
 20 I don't know if that still applies.
 21 Q. Fair enough. You're identified
 22 as -- in the cc's. Do you see that?
 23 A. Yes.
 24 Q. As of this date, did you
 25 consider yourself to be one of the key members

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1 of the team for running the mumps expiry
 2 studies?
 3 MR. SANGIAMO: Object to the
 4 form.
 5 THE WITNESS: I can't say one
 6 way or the other at that time what
 7 preparations we had been making to run
 8 the assay.
 9 BY MR. KELLER:
 10 Q. So you have no recollection as
 11 to -- let me strike that.
 12 You were on the team that
 13 ultimately worked on running the clinical
 14 assays for Protocol 007. Correct?
 15 MR. SANGIAMO: Object to the
 16 form.
 17 MR. KELLER: Let me strike that.
 18 BY MR. KELLER:
 19 Q. You were ultimately on the team
 20 that ran the clinical serum as part of
 21 Protocol 007. Correct?
 22 MR. SANGIAMO: Object to the
 23 form.
 24 THE WITNESS: In the AIGENT, the
 25 mumps AIGENT assay, yes.

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1 BY MR. KELLER:
 2 Q. Did you understand that to be
 3 the mumps expiry studies?
 4 MR. SANGIAMO: Object to the
 5 form.
 6 THE WITNESS: My understanding
 7 was that that was a component of the
 8 mumps expiry study.
 9 BY MR. KELLER:
 10 Q. So at some point you became part
 11 of that team. Correct?
 12 MR. SANGIAMO: Object to the
 13 form.
 14 THE WITNESS: I would say
 15 presumably because I'm copied on this.
 16 BY MR. KELLER:
 17 Q. So when it says the key members
 18 of the team are copied, you just don't know
 19 whether or not you were a key member as of
 20 this date?
 21 A. That's correct. Yes.
 22 Q. But you became a key member at
 23 some point. Correct?
 24 MR. SANGIAMO: Object to the
 25 form.

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1 THE WITNESS: I became a member
 2 of the team. Whether -- a key member
 3 would be a subjective assignment.
 4 BY MR. KELLER:
 5 Q. So you can't -- you can't --
 6 okay.
 7 Who else is cc'd on here? You
 8 have Dr. Ukwu. Who is Kati Abraham, do you
 9 know?
 10 A. I know Kati Abraham or Kati
 11 Abraham, but I don't recall her position at
 12 the time. She has had multiple positions at
 13 Merck.
 14 Q. What was the position that she
 15 had the last time you remember her position?
 16 A. She -- last I recall, she was
 17 overseeing -- I have a general sense of what
 18 she was doing. I don't know what her official
 19 title was or overall responsibilities.
 20 Q. What's your general sense?
 21 A. General sense is something along
 22 the lines of quality control or quality
 23 assurance. And I'm not sure which, within
 24 our -- I don't recall if she was in our --
 25 whatever our department was called at the time

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<p style="text-align: right;">Page 210</p> <p>1 or if she was -- I know she was supporting our 2 department. Whether she was actually part of 3 the department, I don't recall. 4 Q. Did she ever support Protocol 5 007? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: She was at Merck 9 and involved in a quality control/quality 10 assurance role during Protocol 007 to 11 the best of my recollection. 12 BY MR. KELLER: 13 Q. Did you ever interact with her 14 regarding quality control and quality 15 assurance regarding the serum that you ran in 16 Protocol 007? 17 A. I interacted with people in her 18 group. Whether I interacted with her directly, 19 I don't recall. 20 Q. Who did you interact within her 21 group? 22 A. The person, I think it was Leah 23 Gottlieb. 24 Q. What was her position, do you 25 recall?</p>	<p style="text-align: right;">Page 212</p> <p>1 where we had a workbook that were flagged -- 2 for criteria that the workbook was flagging, 3 for example, extravariability is one example, 4 and then helping to identify sera then for a 5 retest. 6 Q. Was that something that you 7 asked her to help with? 8 A. No. 9 Q. Was she -- were you providing 10 results of the clinical studies to her in 11 Protocol 007? Strike that. 12 Were you providing results of 13 experiments to her during the running of 14 Protocol 007? 15 A. Workbooks from Protocol 007 were 16 being provided to her during the running of 17 Protocol 007. 18 Q. And do you know why she was 19 reviewing them? 20 A. I have an, I'll say an 21 understanding of it. I don't know if it's the 22 only reason. 23 Q. What's your understanding? 24 A. Emilio Emini asked how -- I'm 25 sorry. Emilio Emini and Alan Shaw were</p>
<p style="text-align: right;">Page 211</p> <p>1 A. I don't -- to be honest, I don't 2 recall. 3 Q. How did you interact with her, 4 for what purpose? 5 A. Leah, as best I can recall, 6 helped in the SOP review and approval and also 7 served a function in monitoring and reviewing 8 data from the Protocol 007 study. 9 Q. How was she monitoring the data 10 and reviewing the data? For what purpose? 11 Strike that. 12 For what purpose was Leah 13 Gottlieb monitoring the serum in Protocol 007? 14 MR. SANGIAMO: Object to the 15 form. 16 BY MR. KELLER: 17 Q. The data from the serum -- 18 strike that. You're right. 19 Can I get his answer read -- 20 sorry. 21 What -- how was she monitoring 22 and reviewing data for Protocol 007? 23 A. As best I can recall, she was 24 looking through the results spreadsheets 25 identifying sera that were -- in the case</p>	<p style="text-align: right;">Page 213</p> <p>1 looking for someone who could identify sera 2 for -- this is the best of my understanding, 3 for retest, and having Leah look through them 4 allowed more expedited identification of sera 5 for retest. 6 Q. Was that after all the serum was 7 run for Protocol 007 through the experiments? 8 A. It was -- 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: It was -- the 12 reviews were done, as best I can 13 recall, whenever the data were 14 available from a particular experiment 15 or set of experiments. So it was not 16 at the end of a study but at the end of 17 an experiment. 18 BY MR. KELLER: 19 Q. You also testified that she 20 reviewed the SOP. Correct? 21 A. I don't believe I used the term 22 reviewed, but one of her roles was to help in 23 generating and having SOPs approved. 24 Q. How were they -- who approved 25 them?</p>

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<p style="text-align: right;">Page 214</p> <p>1 A. I don't recall who all the 2 approvers were. I don't recall the procedure 3 for review and approval at the time. 4 Q. Do you know why they were 5 approved, why somebody was approving the SOPs? 6 MR. SANGIAMO: Objection. 7 Objection to the form. Calls for 8 speculation. 9 THE WITNESS: I would say that 10 any approval of an SOP was done in 11 order to have the SOP available in an 12 approved form for use. 13 BY MR. KELLER: 14 Q. You don't know what the criteria 15 upon which it was reviewed for and approved? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: I don't recall. 19 I'm not familiar with that. 20 BY MR. KELLER: 21 Q. In Dr. Ukwu's e-mail she writes 22 in the second paragraph, "I would like us to 23 have a firm plan for our assay development and 24 validation prior to their use in any clinical 25 studies to support registration/claim."</p>	<p style="text-align: right;">Page 216</p> <p>1 Q. Did you ever talk to Dr. Ukwu 2 about validating Protocol 007? 3 A. I don't recall talking to her 4 about that. 5 Q. Do you recall talking to anybody 6 about the criteria for validating the AIGENT 7 SOP? 8 MR. SANGIAMO: Object to the 9 form. 10 THE WITNESS: Yes. 11 BY MR. KELLER: 12 Q. Who did you speak to? 13 A. I don't recall. It was someone 14 in biometrics. I don't recall. I'm trying to 15 remember. I'd be guessing, but it was someone 16 in the biometrics group. 17 Q. Do you recall when that happened? 18 A. That, I don't recall. 19 Q. You testified earlier to that 20 person, you just didn't recall. 21 Did you -- and just to go back, 22 did you design the experiments that were going 23 to be used in the validation protocol? 24 A. I contributed to the design of 25 the experiments that were going to be used in</p>
<p style="text-align: right;">Page 215</p> <p>1 Do you see that? 2 A. Yes. 3 Q. And so the assay development, 4 that was something that you did as well for 5 Protocol 007, you did assay development, you 6 developed the AIGENT. Correct? 7 A. I was part of the team that 8 developed the AIGENT assay. 9 Q. And validation, what do you 10 understand validation to mean? 11 A. My understanding of that as 12 written here is that validation would be 13 designing and performing the -- whatever 14 studies were appropriate for a validation 15 plan. 16 Q. So is it fair to say that 17 Dr. Ukwu is saying that she wanted to have a 18 plan for having the validation completed prior 19 to running of any clinical sera in Protocol 20 007? Is that a fair statement here? 21 MR. SANGIAMO: Objection. 22 THE WITNESS: That's what the 23 words say in her e-mail, appear to be 24 saying. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 217</p> <p>1 the validation protocol. 2 Q. What did you contribute? 3 A. I don't recall the specifics. 4 Q. Who else worked on -- was that 5 the person from biometric research who helped 6 identify what experiments would be run as part 7 of the validation protocol? 8 A. As best I can recall, they 9 provided, the biometrics representative or 10 representatives provided guidance as to what 11 sorts of experiments. And, again, I don't 12 remember with certainty but my expectation 13 would be they would give an indication of how 14 many samples, how many runs of the assay, for 15 example. 16 Q. Did you follow their 17 recommendations? 18 A. As best I can recall, yes. 19 Q. Did you run all the experiments 20 that they recommended? 21 A. I'm not aware of any that were 22 recommended that we didn't run, so yes. 23 MR. KELLER: Let me mark this 24 next exhibit as Exhibit 25. 25 - - -</p>

55 (Pages 214 - 217)

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<p style="text-align: right;">Page 218</p> <p>1 (Exhibit Krah-25, Agenda - 2 revision 1, 1614153, was marked for 3 identification.) 4 - - - 5 MR. KELLER: For the record, 6 Exhibit 25 is a single-page document 7 bearing Bates stamp number 1614153, 8 entitled, "AGENDA - Revision 1 Vaccine 9 Tactical PAC June 21, 1999." 10 BY MR. KELLER: 11 Q. What is a -- what is the PAC, do 12 you recall? 13 A. I don't recall. 14 Q. You don't know. Do you recall 15 participating in this meeting on June 21, 16 1999, regarding vaccine tactical PAC? You see 17 at 9:30 there's a discussion of the 18 competitive update for MMR. Do you see that? 19 A. Yes, I see it. 20 Q. You're identified as one of the 21 invitees. Do you see that? 22 A. Yes. 23 Q. Do you recall participating in 24 this meeting? 25 A. I don't recall.</p>	<p style="text-align: right;">Page 220</p> <p>1 I don't have a recollection that I did. 2 Q. Fair enough. There is a 3 reference on the agenda to Nick Spring. Do 4 you know who Nick Spring is? 5 A. I'm sorry? 6 Q. On Exhibit 25. 7 A. I'm sorry, the name Nick Spring? 8 Q. Nick Spring, do you know who 9 Nick Spring is? 10 A. That name is not familiar to me. 11 Q. You don't recall receiving a 12 marketing update at this meeting? 13 A. I don't recall -- I don't recall 14 one. 15 Q. Do you recall receiving a 16 backgrounder in preparation for this meeting? 17 A. I don't recall. 18 Q. Would you be surprised if you -- 19 strike that. 20 MR. KELLER: Let me mark this 21 next exhibit as Exhibit 26. 22 - - - 23 (Exhibit Krah-26, 6/16/99 E-mail 24 with attachments, 285267 - 285296, was 25 marked for identification.)</p>
<p style="text-align: right;">Page 219</p> <p>1 Q. If you could find on -- I've 2 already marked the location of June 21, 1999, 3 in your journals. Can you tell me if you can 4 identify the page that's marked there, the 5 bottom right-hand corner? 6 A. 8615. Page 211 at the top of 7 the report. 8 Q. 0 -- I'm sorry, 48615. Okay. 9 And at 48615, is there a 10 reference for a meeting on June 21, 1999? 11 A. Yes. 12 Q. And what's -- can you tell me 13 what's written there? 14 A. MMR II TPAC presentation 15 9:00 a.m. to 1:00 p.m. Hilleman Conference 16 Room. 17 Q. Can you tell from your journal 18 on that day that you attended this meeting? 19 A. The check mark may suggest that 20 I attended it. 21 Q. If you look on the agenda -- do 22 you have any reason to believe that you didn't 23 attend it? 24 A. I don't have a recollection. I 25 don't have a reason to believe I didn't. But</p>	<p style="text-align: right;">Page 221</p> <p>1 - - - 2 MR. KELLER: Steve and Joanie, 3 can you step out for a minute? 4 For the record, Exhibit 26 is a 5 document that bears Bates stamp number 6 285267 through 285296. There's an 7 e-mail and an attachment, two 8 attachments. The e-mail is dated 9 June 16, 1999, from Joan Staub to a 10 laundry list of people including you, 11 Dr. Krah. 12 BY MR. KELLER: 13 Q. Can you tell me if you recall 14 receiving this backgrounder for the June 21st 15 TPAC meeting? 16 A. I would say it doesn't look 17 familiar to me. 18 Q. If you go to the first page of 19 the e-mail, there's a reference that says, 20 "Attached please find the backgrounder and 21 appendix document for the MMR II Competitive 22 Defense Presentation to the TPAC on June 21." 23 Do you see that? 24 A. Yes. 25 Q. You were a member of the</p>

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<p style="text-align: right;">Page 222</p> <p>1 Competitive Defense Task Force, weren't you?</p> <p>2 A. That I -- I was invited to this</p> <p>3 meeting. Whether I was a member of that, I</p> <p>4 don't know.</p> <p>5 Q. Your counsel has represented</p> <p>6 that you were a member during this time frame.</p> <p>7 Does that refresh your memory that you were a</p> <p>8 member of this particular committee?</p> <p>9 A. I don't recall.</p> <p>10 Q. Have you ever heard of the</p> <p>11 Competitive Defense Task Force before seeing</p> <p>12 this document?</p> <p>13 MR. SANGIAMO: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: I'm sorry, which</p> <p>16 document?</p> <p>17 BY MR. KELLER:</p> <p>18 Q. Let me direct your attention to</p> <p>19 285276, entitled: MMR II Defense Action Plan</p> <p>20 TPAC Background document, prepared by The</p> <p>21 Competitive Defense Task Force for MMR II</p> <p>22 June 1999.</p> <p>23 Do you see that?</p> <p>24 A. Yes.</p> <p>25 Q. Sir, my question for you is, did</p>	<p style="text-align: right;">Page 224</p> <p>1 you were a member of the TPAC. Correct?</p> <p>2 A. I do not recall that.</p> <p>3 Q. You don't remember -- you don't</p> <p>4 recall if you were a member of the Competitive</p> <p>5 Defense Task Force either, do you?</p> <p>6 A. No.</p> <p>7 Q. But you recall being invited to</p> <p>8 meetings where the Competitive Defense Task</p> <p>9 Force gave presentations. Correct?</p> <p>10 A. At least this one example that</p> <p>11 you had I was on the invitee list.</p> <p>12 Q. Let me ask you, sir, why would a</p> <p>13 research scientist be invited to a meeting to</p> <p>14 discuss competitive defense of the MMR II</p> <p>15 vaccine?</p> <p>16 MR. SANGIAMO: Objection.</p> <p>17 Answer if you know.</p> <p>18 THE WITNESS: I don't know.</p> <p>19 BY MR. KELLER:</p> <p>20 Q. And so did you learn about</p> <p>21 Merck's marketing plans for its MMR II</p> <p>22 products at these meetings?</p> <p>23 MR. SANGIAMO: Object to the</p> <p>24 form.</p> <p>25 THE WITNESS: I don't -- there</p>
<p style="text-align: right;">Page 223</p> <p>1 you ever -- you don't -- is it your testimony</p> <p>2 you don't recall being a member of that</p> <p>3 particular task force?</p> <p>4 A. I remember attending or being</p> <p>5 invited to meetings of it, but I don't recall</p> <p>6 if I was -- that I was a member.</p> <p>7 Q. Why would a research scientist</p> <p>8 be invited to -- let me back up a second.</p> <p>9 Strike that.</p> <p>10 Let me direct your attention to</p> <p>11 the third page of the defense action plan at</p> <p>12 285278, under "EXECUTIVE SUMMARY."</p> <p>13 A. Okay.</p> <p>14 Q. The first sentence, it says,</p> <p>15 "The cross-functional defense of MMR II was</p> <p>16 created in 1996 when the Competitive Defense</p> <p>17 Task Force was chartered by TPAC."</p> <p>18 Do you see that?</p> <p>19 A. Yes.</p> <p>20 Q. You don't recall what TPAC</p> <p>21 stands for, do you?</p> <p>22 A. Not at this time. At the time I</p> <p>23 may have known, but I don't recall what it</p> <p>24 stands for.</p> <p>25 Q. You don't recall whether or not</p>	<p style="text-align: right;">Page 225</p> <p>1 may have been information presented on</p> <p>2 that, but I don't recall meaning</p> <p>3 anything to me.</p> <p>4 BY MR. KELLER:</p> <p>5 Q. In the third paragraph it says,</p> <p>6 "Initiatives continue in MRL and MMD to</p> <p>7 ultimately provide a product line which will</p> <p>8 be competitive and satisfy all regulatory</p> <p>9 requirements. Those programs will be updated</p> <p>10 in this background document include:" In</p> <p>11 number 3 is "the defense of Mumps expiry</p> <p>12 titers."</p> <p>13 Do you see that?</p> <p>14 A. Yes.</p> <p>15 Q. Do you recall whether or not</p> <p>16 Protocol 007 was part of this defense of the</p> <p>17 mumps expiry titers?</p> <p>18 A. I don't know whatever the date</p> <p>19 is for this, I don't recall what the status</p> <p>20 of -- whether Protocol 007 existed at that</p> <p>21 time.</p> <p>22 Q. This is June of 1999.</p> <p>23 MR. SANGIAMO: Dr. Krah, you</p> <p>24 should be sure to familiarize yourself</p> <p>25 with the document to the extent you</p>

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<p style="text-align: right;">Page 226</p> <p>1 need to respond to Mr. Keller's</p> <p>2 questions.</p> <p>3 BY MR. KELLER:</p> <p>4 Q. Let me direct your attention to --</p> <p>5 you don't know is what you're saying?</p> <p>6 A. I don't recall the dates.</p> <p>7 MR. SANGIAMO: You don't</p> <p>8 recall the dates.</p> <p>9 BY MR. KELLER:</p> <p>10 Q. Do you recall any discussion,</p> <p>11 irrespective of dates, regarding the use of</p> <p>12 Protocol 007 results in defending mumps expiry</p> <p>13 titers?</p> <p>14 MR. SANGIAMO: Moving away from</p> <p>15 the document?</p> <p>16 MR. KELLER: I'm talking</p> <p>17 generally about the document.</p> <p>18 MR. SANGIAMO: Then, Dr. Krah,</p> <p>19 take your time to familiarize yourself</p> <p>20 with the content --</p> <p>21 BY MR. KELLER:</p> <p>22 Q. I'm talking about one paragraph.</p> <p>23 You want to read the paragraph. If you want</p> <p>24 to go off the record, you can read every</p> <p>25 single page of this document.</p>	<p style="text-align: right;">Page 228</p> <p>1 paragraph?</p> <p>2 Q. Yes. Under "EXECUTIVE SUMMARY."</p> <p>3 MR. SANGIAMO: Dr. Krah, I would</p> <p>4 suggest that you read the executive</p> <p>5 summary in its entirety and look over</p> <p>6 the rest of the document and that will</p> <p>7 be sufficient to answer Mr. Keller's</p> <p>8 question, but we'll see.</p> <p>9 THE WITNESS: Okay.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. My question is, again, do you</p> <p>12 recall ever learning that Protocol 007 was to</p> <p>13 be used as part of the defense of the mumps</p> <p>14 expiry titers as part of Merck's competitive</p> <p>15 defense?</p> <p>16 MR. SANGIAMO: Object to the</p> <p>17 form.</p> <p>18 THE WITNESS: My understanding</p> <p>19 was that Protocol 007 was being used to</p> <p>20 support and characterize MMR whether --</p> <p>21 I'm not -- I don't recall that it was</p> <p>22 part of a -- like a competitive defense</p> <p>23 strategy.</p> <p>24 BY MR. KELLER:</p> <p>25 Q. Fair enough. Look on page 285279</p>
<p style="text-align: right;">Page 227</p> <p>1 MR. SANGIAMO: No, we're not</p> <p>2 going off the record.</p> <p>3 Dr. Krah, read the document to</p> <p>4 the extent necessary to familiarize</p> <p>5 yourself with it.</p> <p>6 MR. KELLER: Let's go off the</p> <p>7 record. I think we should call the</p> <p>8 magistrate at this point. This is</p> <p>9 getting ridiculous.</p> <p>10 MR. SANGIAMO: You're telling</p> <p>11 him he's only allowed to read one</p> <p>12 paragraph of this document?</p> <p>13 MR. KELLER: Sure. He can do it</p> <p>14 off the record. He's going to take</p> <p>15 three hours to read a document, by the</p> <p>16 time --</p> <p>17 MR. SANGIAMO: What makes you</p> <p>18 think it's going to take him three</p> <p>19 hours to read a document?</p> <p>20 BY MR. KELLER:</p> <p>21 Q. Go back on the record.</p> <p>22 Sir, tell me when you're done</p> <p>23 familiarizing yourself with the paragraph that</p> <p>24 I just referenced you.</p> <p>25 A. The initiatives continue</p>	<p style="text-align: right;">Page 229</p> <p>1 under "Marketing Response to SB Competition."</p> <p>2 Do you see that?</p> <p>3 A. Okay. Yes.</p> <p>4 Q. "RESPONSE TO COMPETITION." Do</p> <p>5 you see that at the top of this page?</p> <p>6 A. Yes.</p> <p>7 Q. SB, do you understand that to be</p> <p>8 Smith Barney? I'm sorry, Smith Beecham.</p> <p>9 Sorry, strike that.</p> <p>10 What do you recall SB to stand</p> <p>11 for?</p> <p>12 A. Two paragraphs down it has</p> <p>13 SmithKline Beecham as SB. I don't have a</p> <p>14 recollection of it, but the paragraph just</p> <p>15 before -- or just under the graphs defines</p> <p>16 that SB as SmithKline Beecham.</p> <p>17 Q. Gotcha. Did you understand that</p> <p>18 SmithKline Beecham had its own MMR product</p> <p>19 that it was selling outside the United States</p> <p>20 called Priorix?</p> <p>21 MR. SANGIAMO: Object to the</p> <p>22 form.</p> <p>23 THE WITNESS: I was aware that</p> <p>24 they had one or more vaccines that</p> <p>25 contained measles, mumps and rubella.</p>

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<p style="text-align: right;">Page 230</p> <p>1 I don't recall having familiarity 2 with -- it wasn't being sold in the US. 3 It was being sold outside the US. 4 BY MR. KELLER: 5 Q. Do you recall as part of this 6 presentation in June of 1999 a discussion 7 about Priorix and its threat of Priorix coming 8 to the US market? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: In reading through 12 the document, at the beginning of the 13 discussion I recall seeing sections 14 that comment on that aspect of the 15 GSK -- I'm sorry, the SmithKline 16 Beecham vaccine being a competitive 17 threat to the MMR vaccine. 18 BY MR. KELLER: 19 Q. Do you recall -- other than 20 reading this document today, do you recall any 21 discussions about it back in 1999? 22 A. At least one aspect to it, yes. 23 Q. What is that? 24 A. When we did -- conducted the 25 Protocol 006 study which was a head-to-head</p>	<p style="text-align: right;">Page 232</p> <p>1 CBER that -- so I don't -- it's correct I 2 don't know the overall study goals, but I do 3 know from discussion with CBER that a 95 4 percent seroconversion was a requirement. 5 Q. And that requirement of 95 6 percent, do you understand that that was what 7 was represented in the then current label of 8 MMR II for mumps? 9 A. I don't recall. 10 Q. Just that they wanted 95 percent 11 seroconversion in a neutralizing assay. 12 Correct? 13 A. Yes. 14 Q. What were the goals of Protocol 15 007? I mean, sorry. What were the -- strike 16 that. 17 What were the goals of Protocol 18 006? 19 A. I have a -- my perspective or my 20 understanding of the goals in the same context 21 of Protocol 007, there may have been other 22 study goals than are beyond what I was 23 thinking, the goals that I was aware of were 24 comparing the immunogenicity of the mumps 25 component of MMR and Priorix against different</p>
<p style="text-align: right;">Page 231</p> <p>1 study of MMR with Priorix, that was, from my 2 understanding, a competitive trial to compare 3 immunogenicity of the mumps component of MMR 4 with Priorix. 5 Q. They may have used a plaque 6 reduction neutralization assay in that study. 7 Correct? 8 A. Yes. 9 Q. That study, that was Protocol 10 006. Correct? 11 A. Yes. 12 Q. That study didn't use any 13 anti-IgG steps, did it? 14 A. That's correct. 15 Q. Which assay do you think is a 16 better assay for showing immunogenicity, the 17 AIGENT or the assay used in Protocol 006? 18 A. Let me tell you, it depends on 19 the goals of the study. I would say both are 20 equally relevant and important. So at 1.1 is 21 better than the other. 22 Q. When you say the goals of the 23 study, you testified that you didn't know what 24 the goals were for the Protocol 007. Correct? 25 A. I knew from discussions with</p>	<p style="text-align: right;">Page 233</p> <p>1 wild type mumps strains to see if there's a 2 difference in the breadth of neutralization 3 induced by MMR versus Priorix. 4 Q. What do you mean by 5 "immunogenicity"? 6 A. Neutralization results, meaning 7 there are two, at least as best I can recall, 8 two sets -- two forms of data that were 9 provided in Protocol 006. One is a 10 seroconversion rate. The other is a geometric 11 mean titer. So from an immunogenicity 12 standpoint I put those both in as 13 immunogenicity measures that were part of 14 Protocol 006. 15 Q. Was Protocol 006 designed to 16 determine whether or not kids would be 17 protected from mumps? 18 A. Not -- not to my understanding, 19 but I wasn't -- it's beyond my scope of 20 responsibility. I had no awareness that it 21 was designed to show protection. 22 Q. If you go back to Exhibit 26. 23 In the second paragraph it says, MMR is 24 currently an exclusive license in the United 25 States.</p>

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<p style="text-align: right;">Page 234</p> <p>1 Do you see that?</p> <p>2 A. I'm sorry, what page?</p> <p>3 Q. 285279, the same page we were</p> <p>4 on.</p> <p>5 A. Okay.</p> <p>6 Q. Do you recall a discussion at</p> <p>7 this --</p> <p>8 A. Could you repeat that?</p> <p>9 Q. Sure. In the first sentence it</p> <p>10 says, MMR II is currently the exclusive</p> <p>11 vaccine in the United States...</p> <p>12 Do you see that?</p> <p>13 A. Yes.</p> <p>14 Q. Do you recall any discussion</p> <p>15 about that statement in June of 1999 at this</p> <p>16 meeting?</p> <p>17 A. I don't -- yeah, I don't recall?</p> <p>18 Q. Do you recall whether or not</p> <p>19 there are any other mumps, measles and rubella</p> <p>20 vaccines being sold in the United States as of</p> <p>21 1999?</p> <p>22 A. I would say I wasn't aware of</p> <p>23 any others, but I'm not an expert in the area.</p> <p>24 Q. Are you aware of any other MMR</p> <p>25 vaccines that are being sold in the US today?</p>	<p style="text-align: right;">Page 236</p> <p>1 The objectives of the Marketing element of</p> <p>2 MMR II Competitive Defenses are to, in 1,</p> <p>3 "Pursue a proactive tactical plan including</p> <p>4 initiatives to delay and disrupt the launch of</p> <p>5 Priorix into the market."</p> <p>6 Do you see that?</p> <p>7 A. Yes.</p> <p>8 Q. Do you recall any discussion at</p> <p>9 this meeting regarding that tactical plan to</p> <p>10 prevent Priorix from entering the market?</p> <p>11 A. I do not.</p> <p>12 Q. Have you ever discussed that</p> <p>13 with anybody at Merck outside of this</p> <p>14 presentation?</p> <p>15 A. As part of the Protocol 006</p> <p>16 study I would say yes, because my understanding</p> <p>17 of the study was a potential first step in</p> <p>18 trying to show whether MMR was superior to</p> <p>19 Priorix in protecting from a range of</p> <p>20 different viruses.</p> <p>21 Q. I thought you just testified</p> <p>22 that Protocol 006 had nothing to do with</p> <p>23 determining whether or not it was protective</p> <p>24 against disease. I'm confused.</p> <p>25 MR. SANGIAMO: Hold on a second.</p>
<p style="text-align: right;">Page 235</p> <p>1 A. I am not aware of any.</p> <p>2 Q. Are you aware of any MMR</p> <p>3 vaccines being sold in the US between 1999 and</p> <p>4 today?</p> <p>5 A. I'm not aware of any.</p> <p>6 Q. Have you ever used the term</p> <p>7 "exclusive license" in any of your</p> <p>8 communications with anybody?</p> <p>9 A. Yes.</p> <p>10 Q. Can you -- when have you used</p> <p>11 that term?</p> <p>12 A. Early -- one example is if</p> <p>13 we're -- for example, a scientist outside</p> <p>14 Merck has a method or reagent that we're</p> <p>15 interested in, we might consider engaging in</p> <p>16 an exclusive license so Merck would be the</p> <p>17 only organization to which they would license</p> <p>18 the product, or the method or reagent.</p> <p>19 Q. Do you recall ever discussing</p> <p>20 with anybody that Merck's MMR product, that</p> <p>21 they had -- that Merck had an exclusive</p> <p>22 license for MMR II in the US?</p> <p>23 A. I do not recall discussing that</p> <p>24 with anyone.</p> <p>25 Q. In the next paragraph it says,</p>	<p style="text-align: right;">Page 237</p> <p>1 What's your question?</p> <p>2 BY MR. KELLER:</p> <p>3 Q. So my question is, can you</p> <p>4 explain yourself, what you mean?</p> <p>5 MR. SANGIAMO: What he means by</p> <p>6 what, I'm sorry?</p> <p>7 BY MR. KELLER:</p> <p>8 Q. The differences between</p> <p>9 protection in discussion of Protocol 006 and</p> <p>10 your discussion testimony earlier that</p> <p>11 Protocol 006, as you understand it, was not</p> <p>12 linked to protection from disease?</p> <p>13 MR. SANGIAMO: Object to the</p> <p>14 form.</p> <p>15 THE WITNESS: It was not -- the</p> <p>16 study Protocol 006 was not, to my</p> <p>17 understanding, designed to evaluate</p> <p>18 protection. But from a scientific</p> <p>19 standpoint, the concept of one vaccine</p> <p>20 giving higher seroconversion rate and</p> <p>21 geometric mean titer to a wider range</p> <p>22 of viruses would be suggestive or</p> <p>23 indicated in vitro at least one vaccine</p> <p>24 versus the other would be able to</p> <p>25 produce a more broadly neutralizing set</p>

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1 of antibodies. It's not a direct
 2 indicator or measure of protection but
 3 suggestive of a broader in vitro
 4 capacity of sera from the one --
 5 generated by one vaccine to induce a
 6 different quality antibody.
 7 BY MR. KELLER:
 8 Q. Do you recall how many different
 9 wild type viruses you tested?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: I don't recall
 13 specifically. I know at least two. I
 14 don't remember the exact number.
 15 BY MR. KELLER:
 16 Q. You say -- my question is, how
 17 many you actually tested, not how many you
 18 reported. Did you only test two wild type
 19 viruses or did you test more than two wild
 20 type viruses and only report two?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: We reported
 24 results for all the viruses that we
 25 tested in Protocol 006.

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1 BY MR. KELLER:
 2 Q. Was there ever discussion about
 3 testing more than those two wild type viruses?
 4 MR. SANGIAMO: Object to the
 5 form.
 6 THE WITNESS: As best I can
 7 recall, there was both discussion and
 8 an initial plan, at least on my part,
 9 to look at additional viruses.
 10 BY MR. KELLER:
 11 Q. Why didn't you look at
 12 additional viruses? Who made the decision not
 13 to look at additional viruses?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: I can't say for
 17 certainty. My understanding was -- my
 18 recollection is it was a team decision.
 19 BY MR. KELLER:
 20 Q. What were the pros and cons in
 21 looking at more wild types versus the ones you
 22 decided upon?
 23 MR. SANGIAMO: Object to the
 24 form.
 25 THE WITNESS: The interest in

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1 looking at additional wild type viruses
 2 would be to gather more information
 3 about comparisons between the MMR
 4 vaccine and Priorix. I wouldn't count
 5 this as a con, but the negative aspect,
 6 which is my understanding of why we
 7 didn't proceed, was that there wasn't
 8 sufficient vials of sera to test
 9 additional viruses. We had a limited
 10 volume of sera from the pediatric
 11 samples. For each virus that you test,
 12 there's more of a serum volume that you
 13 need to use.
 14 BY MR. KELLER:
 15 Q. Didn't you use sera from
 16 Protocol 006 to test, to develop the protocol
 17 for Protocol 007?
 18 A. I don't recall if -- that we
 19 did.
 20 Q. You could have, you just don't
 21 remember?
 22 A. I don't remember. If we did, I
 23 would offer if we did use it, the Protocol 007
 24 study required a much smaller volume of sera
 25 than Protocol 006. So I would expect cases

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1 where there's insufficient volume to do more
 2 testing in Protocol 006 but would be
 3 sufficient volume to use in an assay that used
 4 less volume.
 5 MR. KELLER: Mark this next
 6 exhibit.
 7 - - -
 8 (Exhibit KraH-27, Handwritten
 9 note, 448146, was marked for
 10 identification.)
 11 - - -
 12 BY MR. KELLER:
 13 Q. Exhibit 27 which is a document
 14 that bears Bates number 448 -- 448146, 448146.
 15 Sir, can you tell me what this document is?
 16 A. It's a page indicated purpose of
 17 a study involving a mumps neutralization
 18 assay.
 19 Q. And there is a book and page
 20 number on this. What does that mean to you?
 21 Can you describe what that means?
 22 A. Yes. The book would be a
 23 combination of numbered pages.
 24 Q. Is this part of a -- would this
 25 go into a -- why would the pages be -- why

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1 would this be written into a book on a page?
 2 Explain that to me.
 3 MR. SANGIAMO: Objection.
 4 BY MR. KELLER:
 5 Q. Strike that. Let me start over.
 6 What was the purpose of having a
 7 book and page?
 8 A. This was part of our general
 9 notebook policy of having a uniquely numbered
 10 book and page for documenting the experiments.
 11 Q. Here it says, Project Number
 12 V205C. That's a reference to MMR II. Correct?
 13 A. That is a project code that has
 14 been used previously for MMR II.
 15 Q. Under "Project Page" it says,
 16 "MMR/V 80-99."
 17 Do you see that?
 18 A. Yes.
 19 Q. That identifies the experiment.
 20 Correct?
 21 A. That -- it's a unique a
 22 combination of letters and numbers and year
 23 that identify -- it's a shorthand that was
 24 used to identify the experiment.
 25 Q. And MMR/V, I've noticed

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1 throughout all the experiments that I've
 2 reviewed from the record, they all have MMR/V
 3 and not MMR for Protocol 007. Can you explain
 4 to me why that is?
 5 A. Yes. The basis for this, when I
 6 started the lab, we had and continued to work
 7 on different viruses, so we had different
 8 codes for different sets of viruses. For
 9 example, hepatitis A might be HAV and then a
 10 number. Many experiments we were doing
 11 included measles, mumps, rubella or varicella
 12 so we needed a catchall MMR/V. So it could
 13 include something that's measles, something
 14 that's mumps, something that's rubella,
 15 something that's varicella.
 16 Q. So that's just a grouping within
 17 that sort of -- for that product line.
 18 Correct? Is that fair?
 19 A. It's more -- I would characterize
 20 it as a grouping, a convenience grouping for
 21 in the lab, for example, if we were doing work
 22 with rotavirus, we might have a rota 1-1-99 or
 23 MMR/V-1-99. So it's a -- it's a convenient
 24 grouping, I don't know if you call it by
 25 product because some of the projects weren't

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1 products, but it's a way of grouping
 2 experiments by family of viruses or group of
 3 viruses.
 4 Q. Fair enough. In the first
 5 number, did you number all of the experimental
 6 -- experiments you did in developing Protocol
 7 007? Did you start from one and went through
 8 whatever the end number is?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: The numbering
 12 system, as best I recall, for all
 13 experiments that are being done in the
 14 lab, they're not unique to one
 15 particular like Protocol 006 or any
 16 other protocol.
 17 BY MR. KELLER:
 18 Q. And then the last two numbers
 19 are just the year that it's running?
 20 A. Yes.
 21 Q. Here it says, "Investigator,"
 22 what does that mean?
 23 A. That means that that's the
 24 person who was involved in running the
 25 experiment, writing up the experiment.

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1 Q. So that's the person that
 2 actually wrote up this page, was you?
 3 A. Yes.
 4 Q. And that's your handwriting?
 5 A. Yes.
 6 Q. And then it says, "Subject."
 7 What is the purpose of the subject line?
 8 A. The subject -- purpose of the
 9 subject line is to give a descriptive summary
 10 of the experiment that then can be put in an
 11 index and someone looking through the index
 12 could identify what the -- what that
 13 experiment referred -- relates to.
 14 Q. Is it just sort of a general
 15 statement of what is followed in the details?
 16 A. Yes, descriptive, the attempt is
 17 the goal is to be a descriptive general
 18 statement about what follows.
 19 Q. Gotcha. And then under "Filed
 20 in Book Number/Title," what is the purpose of
 21 that field?
 22 A. The notebooks, which were paper
 23 notebooks, we would put in three-ring binders
 24 typically. The three-ring binders were
 25 labeled by year and then letter, for example,

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<p style="text-align: right;">Page 246</p> <p>1 1999, if we had four binders, we would have an 2 A, B, C, D. 3 Q. It just helped you find the 4 actual experiment in the binder? 5 A. Yes. It tells you what binder 6 it's in. 7 Q. This particular experiment, you 8 ran this -- it says date February 6, 1999? 9 A. Yes. 10 Q. So, if you recall, the Protocol 11 007 -- in Protocol 007 I showed you earlier in 12 Exhibit 22, that was done on February 2, 1999. 13 So this was done a couple of days after that 14 protocol was finalized? 15 MR. SANGIAMO: Exhibit 22. 16 BY MR. KELLER: 17 Q. Strike that. So the protocol 18 that is in Exhibit 22 I recall you testified 19 you don't recall seeing this one. This one 20 was dated February 2, 1999. Do you see that 21 at the bottom? It's on every page, so you 22 can't miss it. 23 A. Okay. 24 Q. Do you see that? 25 A. Yes.</p>	<p style="text-align: right;">Page 248</p> <p>1 experiment? 2 A. Yes. It says purpose to 3 "determine the capacity of antihuman IgG 4 antibody to enhance mumps neutralizing 5 activity of a human serum. A low-positive (by 6 nonenhanced neutralization assay) serum is 7 being tested in this pilot experiment." 8 Q. When you say "pilot experiment," 9 what do you mean by pilot? 10 A. Pilot means it's an initial 11 early probe experiment to look for a 12 phenomenon to try to answer a general question 13 without going into our yet defining multiple 14 variables that could be considered. But just 15 to see like, in this case, if there's a 16 question of does the anti-human IgG antibody 17 enhance mumps neutralization activity, yes or 18 no. And if it's yes, then design additional 19 experiments to do further development. If no, 20 consider why it might not have worked if it 21 was expected to work or just say it didn't 22 work, end of story. 23 Q. Why were you looking at 24 antihuman IgG at this time frame, do you 25 recall?</p>
<p style="text-align: right;">Page 247</p> <p>1 Q. So this experiment that you ran 2 in Exhibit 27 was done a couple of days after 3 that protocol was drafted. Correct? 4 MR. SANGIAMO: Object to the 5 form. Calls for speculation. 6 THE WITNESS: The dates say that 7 the experiment was done a couple of 8 days after that protocol was approved. 9 BY MR. KELLER: 10 Q. And so is it fair to say was 11 this experiment, this experiment related to 12 Protocol 007 in Exhibit 27? 13 A. I can't say with certainty. My 14 expectation is that it would because it 15 included anti-IgG. I don't recall other 16 experiments that we were doing at the time. 17 Q. Do you recall preparing for a 18 meeting with CBER to discuss the methodology 19 for running the neutralization assay in this 20 time frame? 21 A. I don't recall the time -- I 22 recall preparing for a meeting with CBER, but 23 I don't recall the time frame. 24 Q. Could you read your handwriting 25 for the purpose of this particular lab</p>	<p style="text-align: right;">Page 249</p> <p>1 A. At this time I don't -- I can't 2 say with certainty why it was being looked at 3 at that time. 4 Q. Were you considering using it as 5 part of Protocol 007 at this time? 6 A. It was being considered after 7 discussion with the FDA or CBER on including 8 it in Protocol 007. Whether that at this time 9 matches that, I don't recall. 10 Q. Why were you focusing here on -- 11 in my review of your files, this is the first 12 experiment that I could find where you were 13 investigating antihuman IgG. Do you recall 14 doing any experiments prior to this date? 15 A. I don't recall. 16 MR. SANGIAMO: Object to the 17 form. 18 BY MR. KELLER: 19 Q. Do you recall -- when do you 20 recall the first time you considered using an 21 antihuman IgG in a plaque reduction 22 neutralization assay? 23 A. For mumps? 24 Q. For any purposes. 25 A. Early to mid-1990s.</p>

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1 Q. And you used that in a different
2 vaccine?
3 A. Yes.
4 Q. That was used in varicella.
5 Correct?
6 A. Yes.
7 Q. And so in varicella you used
8 anti-IgG with complement. Correct?
9 A. Yes.
10 Q. Why?
11 A. The two -- in evaluation of the
12 anti-IgG and complement, it was found that
13 both had enhancing effect to neutralization
14 but the two together had an -- the two
15 together had an increased enhancement versus
16 either alone.
17 Q. Did you try that with the mumps
18 virus -- strike that.
19 Did you try that with the PRN
20 assay for mumps using both the complement and
21 the anti-IgG step?
22 A. We evaluated complement. I
23 don't recall that we evaluated complement and
24 anti-IgG together.
25 Q. Why were you focused on low

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1 positives in this experiment?
2 A. I don't recall.
3 Q. So it appears as a low positive
4 by non-enhanced neutralization assay. Did you
5 test that same sample in a standard
6 neutralization assay and compare it to a --
7 the assay using the anti-IgG still?
8 A. I can't say for certain what's
9 written here. The wording implies that it
10 was -- there was a result from using the
11 non-enhanced neutralization assay.
12 Q. When you say "neutralization
13 assay," what do you mean by that?
14 A. What I mean by that --
15 MR. SANGIAMO: Object to the
16 form. You can answer.
17 THE WITNESS: -- reduction,
18 percent reduction in plaque relative to
19 those serum control.
20 BY MR. KELLER:
21 Q. What's the serum control?
22 A. Typically a sample with virus
23 and no antibody. Incubated in the same
24 conditions as the antibody-containing samples.
25 Q. So a mock control?

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1 A. It's like often referred to as a
2 no serum control. One could call it a mock
3 control, but I'd call it a no serum control
4 typically.
5 Q. So you would take the medium
6 antihuman IgG and virus and see what happens?
7 MR. SANGIAMO: Object to the
8 form.
9 BY MR. KELLER:
10 Q. I'm trying to understand what
11 you mean.
12 A. So it would be -- it's a
13 sequential -- kind of a small technical
14 detail. It's a sequential addition, meaning
15 the virus and antibody is incubated first and
16 then anti-IgG is added later.
17 The incubation is a sequential
18 incubation of virus plus antibody or in this
19 case no anti -- serum or culture medium alone,
20 no sera. And then anti-IgG is added. So the
21 no serum control would be the virus, culture
22 medium, which is the diluent, and the assay
23 and then anti-IgG.
24 Q. Did you ever discuss with
25 anybody what an appropriate control would be

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1 for using the anti-IgG step?
2 MR. SANGIAMO: Object to the
3 form.
4 THE WITNESS: I don't recall any
5 specific discussion over what others
6 thought might -- would be appropriate
7 controls.
8 BY MR. KELLER:
9 Q. Do you recall ever meeting with
10 the FDA and asking them what appropriate
11 controls would be for plaque reduction
12 neutralization assay?
13 A. I recall meeting with the FDA
14 talking about what controls we had in the
15 plaque reduction neutralization assay. They
16 did not have any other recommendations that I
17 can recall.
18 MR. KELLER: Let me mark this
19 next exhibit as Exhibit 28.
20 - - -
21 (Exhibit Krah-28, 2/24/99 E-mail
22 with attachments, 95046 - 95053, was
23 marked for identification.)
24 - - -
25 MR. KELLER: For the record,

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<p style="text-align: right;">Page 254</p> <p>1 Exhibit 28 is a document that bears 2 Bates stamp number 95046 through 53. 3 The first page is an e-mail from 4 Dr. Chirgwin, dated February 24, 1999, 5 subject: MMR II; Summary of FDA 6 conversation (February 19, 1999). 7 BY MR. KELLER: 8 Q. Sir, you are one of the 9 recipients of this document. Want to take a 10 minute and take a look at the document and the 11 attachments. 12 I want to just start with the 13 first document. We can -- 14 MR. SANGIAMO: He's not done. 15 MR. KELLER: He can read the 16 other ones when we get to it. 17 MR. SANGIAMO: No, no, no. No. 18 It's an exhibit, he's reading the 19 exhibit. 20 MR. KELLER: Sure. 21 BY MR. KELLER: 22 Q. Let me know when you're done. 23 A. Okay. 24 Q. Do you recall receiving this 25 e-mail and the attachments?</p>	<p style="text-align: right;">Page 256</p> <p>1 Do you see that? 2 A. Yes. 3 Q. Are you familiar with formal FDA 4 minutes and non-formal FDA minutes? 5 A. No. 6 MR. SANGIAMO: Object to the 7 form. 8 BY MR. KELLER: 9 Q. Did you have an understanding 10 that -- did you have an understanding of this 11 rule that required the FDA to generate 12 meeting -- formal meetings? 13 MR. SANGIAMO: Object to the 14 form. 15 MR. KELLER: Strike that. 16 BY MR. KELLER: 17 Q. Did you have an understanding of 18 the rules that the FDA had to follow for 19 producing formal minutes of meetings? 20 A. No. 21 Q. Let me turn your attention to 22 the actual meeting minutes of the FDA of 23 February 19th. It's on 59 -- 95048. It 24 identifies you, sir, as being one of the 25 participants. You recall participating in</p>
<p style="text-align: right;">Page 255</p> <p>1 A. Parts of it look familiar to me. 2 Q. Which parts look familiar? 3 A. The description or summary of 4 the CBER method. I don't recall -- that's the 5 main part. I don't recall specifics of the -- 6 the important questions or the -- I remember 7 discussion of the challenge virus of how many 8 plaques they were using -- platform units they 9 were using. But I don't recall the specific 10 numbers they have listed here. 11 Q. If you look on the second page 12 of the e-mail it says, "Attached is a memo 13 summarizing a teleconference with the FDA last 14 Friday during which the methods for the mumps 15 neutralizing antibody assay were discussed. 16 "Also attached is a fax provided 17 by CBER which briefly outlines their assay 18 methods. 19 "Under PDUFA Roman numeral II, 20 the FDA is charged with producing meeting 21 minutes." 22 Do you see that? 23 A. Yes. 24 Q. "Attached below is a fax of the 25 meeting minutes provided by CBER."</p>	<p style="text-align: right;">Page 257</p> <p>1 this meeting. Correct? 2 A. I recall a discussion. I 3 don't -- the CBER method description looks 4 familiar to me. So I assume I was there, but 5 I can't say that I remember with 100 percent 6 certainty that I was there. 7 Q. Do you have any reason to 8 believe that you weren't there since the FDA 9 identified you there at this meeting? 10 A. No. 11 MR. SANGIAMO: Object to the 12 form. 13 BY MR. KELLER: 14 Q. If you look at the first 15 sentence it says, "Merck wanted to discuss 16 their plaque reduction neutralization assay." 17 And in the second bullet point it says, They 18 want to compare their assay procedure with 19 CBER's assay. 20 Do you see that? 21 A. Yes. 22 Q. Do you recall comparing your 23 assay with CBER's plaque reduction 24 neutralization assay? 25 A. I recall discussion of the</p>

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<p style="text-align: right;">Page 258</p> <p>1 procedural differences between our assays. I 2 don't recall at that time physically comparing 3 the two assays. 4 Q. Under the "CBER method" it says 5 in the second bullet, "Uses no complement or 6 immunoglobulin." 7 Do you see that? 8 A. Yes. 9 Q. And immunoglobulin would include 10 the anti-IgG step. Correct? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: Anti-IgG would be 14 an immunoglobulin. 15 BY MR. KELLER: 16 Q. Do you recall discussing the use 17 of the anti-IgG step at this particular 18 meeting? 19 A. That, I don't recall. 20 Q. Do you recall CBER saying that 21 they didn't think that maneuver was necessary? 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: I do not recall 25 them saying that it was not necessary.</p>	<p style="text-align: right;">Page 260</p> <p>1 the protocol discussion that was used at the 2 investigator's meeting where they talked about 3 using the Tennessee virus. Do you recall 4 whether or not Merck first contemplated using 5 the Tennessee strain? 6 MR. SANGIAMO: You didn't show 7 that in protocol. You showed him a 8 slide that mentioned the Tennessee 9 virus. 10 BY MR. KELLER: 11 Q. Go ahead. 12 MR. SANGIAMO: So what was your 13 question? 14 BY MR. KELLER: 15 Q. You can answer. 16 MR. SANGIAMO: The question is 17 do you recall whether or not Merck 18 first contemplated using the Tennessee 19 strain. So I object -- if that's the 20 question, I object to the form. 21 MR. KELLER: Fine. 22 BY MR. KELLER: 23 Q. You can answer. 24 A. I don't recall. 25 Q. The second question says, "What</p>
<p style="text-align: right;">Page 259</p> <p>1 The assay that they were running did 2 not use it. But they did not say it 3 wasn't necessary for our application. 4 BY MR. KELLER: 5 Q. You don't recall them saying 6 that it should not be necessary for running 7 the assay that you guys were going to run for 8 Protocol 007? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: I don't recall 12 that they said that. 13 BY MR. KELLER: 14 Q. Okay. Let's go on. It goes 15 on -- there are two important questions, do 16 you see that, in CBER's meeting minutes? 17 A. Okay. Yes. 18 Q. And the first one is, "What is 19 the wild type strain of virus used?" 20 Do you see that? 21 A. Yes. 22 Q. In this case it is the Tennessee 23 strain. Do you see that? 24 A. Yes. 25 Q. We've shown you -- I showed you</p>	<p style="text-align: right;">Page 261</p> <p>1 is the appropriate control?" 2 Do you see that? 3 A. Yes. 4 Q. Do you recall what was discussed 5 about what appropriate control would be used 6 for a plaque reduction neutralization assay? 7 MR. SANGIAMO: At this meeting? 8 MR. KELLER: At this meeting. 9 THE WITNESS: At this meeting I 10 recall there -- well, that they have 11 written here the immunoglobulin number 12 176 as a positive control. I don't see 13 a comment here about media -- response 14 to the media or negative human serum. 15 In our studies we use a media control. 16 I don't recall that CBER suggested an 17 alternative of an additional negative 18 control. 19 BY MR. KELLER: 20 Q. So you don't know this reference 21 here, where it says media or negative serum, 22 human serum? Do you see that? 23 A. I see that, yes. 24 Q. You don't recall what was 25 discussed about that?</p>

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<p style="text-align: right;">Page 262</p> <p>1 A. No.</p> <p>2 Q. And you never attempted to use a</p> <p>3 negative human serum control. Correct?</p> <p>4 MR. SANGIAMO: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: We did not have</p> <p>7 access to a negative serum control, as</p> <p>8 best I understand.</p> <p>9 BY MR. KELLER:</p> <p>10 Q. When you say that a positive</p> <p>11 serum control, what is that?</p> <p>12 A. That means a serum that is</p> <p>13 positive for which a titer could be measured</p> <p>14 so that one can monitor titer across assays.</p> <p>15 Q. Did you use that as a control?</p> <p>16 MR. SANGIAMO: Object to the</p> <p>17 form.</p> <p>18 BY MR. KELLER:</p> <p>19 Q. As part of the AIGENT?</p> <p>20 A. We did not use immunoglobulin</p> <p>21 number 176 in the AIGENT assay but we had</p> <p>22 additional positive controls that CBER agreed</p> <p>23 to.</p> <p>24 Q. CBER required?</p> <p>25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 264</p> <p>1 using, proposed using, including the controls,</p> <p>2 was provided to Merck and CBER for review.</p> <p>3 I'm not aware that there was any -- so it was</p> <p>4 provided to others for review and comment, and</p> <p>5 I don't recall any additional controls that</p> <p>6 they requested.</p> <p>7 Q. Did anybody other than yourself</p> <p>8 determine what controls would be proposed to</p> <p>9 CBER?</p> <p>10 A. I'm not aware of others. I</p> <p>11 recall proposing the controls that we planned</p> <p>12 for the assay. I can't exclude that someone</p> <p>13 else might have proposed another that was not</p> <p>14 included.</p> <p>15 Q. I see. Fit for purpose, do you</p> <p>16 know where that comes from? Is that an</p> <p>17 industry standard?</p> <p>18 MR. SANGIAMO: Objection. You</p> <p>19 can answer.</p> <p>20 THE WITNESS: So I can't say at</p> <p>21 the time whether it was a phrase that</p> <p>22 was used often, but in the current</p> <p>23 group that I'm in, when an assay is</p> <p>24 being developed, a characteristic -- or</p> <p>25 an objective to the assay is fit for</p>
<p style="text-align: right;">Page 263</p> <p>1 form.</p> <p>2 THE WITNESS: They were part of</p> <p>3 the assay and CBER required limits on</p> <p>4 those. As far as I understand, they</p> <p>5 were part of the assay. CBER required</p> <p>6 limits on them.</p> <p>7 BY MR. KELLER:</p> <p>8 Q. Do you understand what is meant</p> <p>9 by appropriate control?</p> <p>10 MR. SANGIAMO: Objection. Calls</p> <p>11 for speculation.</p> <p>12 THE WITNESS: It's a -- it would</p> <p>13 be a fit-for-purpose application,</p> <p>14 meaning that controls would be -- what</p> <p>15 controls apply would be dependent on</p> <p>16 the assay and a precedent.</p> <p>17 BY MR. KELLER:</p> <p>18 Q. In this fit-for-purpose</p> <p>19 application, did anybody evaluate the AIGENT</p> <p>20 for its fit for purpose in the controls used?</p> <p>21 MR. SANGIAMO: Object to the</p> <p>22 form.</p> <p>23 BY MR. KELLER:</p> <p>24 Q. Or was that just you?</p> <p>25 A. The procedure that we were</p>	<p style="text-align: right;">Page 265</p> <p>1 purpose meaning that the assay meets</p> <p>2 the expectations as far as</p> <p>3 reproducibility or other validity</p> <p>4 criteria that are needed for the</p> <p>5 application.</p> <p>6 BY MR. KELLER:</p> <p>7 Q. And so -- but you didn't know</p> <p>8 what the objective of Protocol 007 was, you</p> <p>9 only knew one component of that objective</p> <p>10 which you say was a comparison of the vary --</p> <p>11 the three different doses. Correct?</p> <p>12 A. Yes.</p> <p>13 Q. So the other purposes you didn't</p> <p>14 know. Correct? The other objectives you</p> <p>15 didn't know?</p> <p>16 A. Yes, that's correct.</p> <p>17 Q. So this surrogate of efficacy,</p> <p>18 that objective, you weren't aware of that.</p> <p>19 Correct?</p> <p>20 MR. SANGIAMO: Object to the</p> <p>21 form.</p> <p>22 THE WITNESS: At least I don't</p> <p>23 recall that being or wasn't -- don't</p> <p>24 recall being aware of that objective.</p> <p>25 BY MR. KELLER:</p>

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<p style="text-align: right;">Page 266</p> <p>1 Q. So if you weren't aware of it, 2 you cannot make a determination of the 3 controls were fit for purpose of your AIGENT 4 you developed if you didn't know all the 5 objectives, could you? 6 A. I wouldn't have all the 7 information, but the information was provided 8 to others who would have that information, and 9 they did not make a contrary recommendation. 10 Q. Who was it provided that would 11 make those -- that determination? 12 A. CBER amongst the group. 13 Q. What about internally at Merck? 14 A. Internally at Merck, I don't 15 know who the -- there was a clinical assay 16 sub-team I recall that was a group to which 17 the assay development was -- updates were 18 provided to them on the assay development. 19 Q. Is that a management team that 20 reviews assays for fit for purposes? 21 A. It's a group that develops, the 22 best of my recollection, clinical assays. I 23 don't -- I can't speak to what their overall 24 responsibilities are, but at that group, 25 clinical assays in development would be</p>	<p style="text-align: right;">Page 268</p> <p>1 Q. Do you recall anybody? 2 A. I couldn't pull a name out of 3 the air. 4 Q. Let me turn your attention to 5 the memo dated February 22, 1999, that was 6 attached to Dr. Chirgwin's e-mail to you, 7 Dr. KraH. Do you recall receiving this memo 8 from Dr. Chirgwin to Dr. Ukwu summarizing the 9 meeting with the FDA? 10 A. There are lines in it where the 11 topic looks familiar, but I can't say the 12 document overall is familiar to me. 13 Q. Was it Merck's practice to 14 create internal memos of meetings with CBER? 15 MR. SANGIAMO: Answer if you 16 know obviously. 17 THE WITNESS: I don't -- 18 BY MR. KELLER: 19 Q. Have you -- sorry, I didn't mean 20 to interrupt you. 21 A. There are meetings where there 22 are -- there have been, not necessarily mumps 23 specific, but there have been internal 24 minutes, but I don't know what the Merck 25 practice was.</p>
<p style="text-align: right;">Page 267</p> <p>1 discussed and discussions would be held, 2 include discussions over whether the assay was 3 meeting the requirements. 4 Q. Were you a member of that group? 5 A. I remember attending the 6 meetings. Whether I was actually a member of 7 it, I can't say. 8 MR. SANGIAMO: Jeff, I know it's 9 unintentional, but I think you're 10 starting in with some of your questions 11 before letting Dr. KraH finish his 12 answer. And you commented at the 13 beginning about sometimes there would 14 be a pause before somebody completes. 15 I just ask that you work harder in 16 trying to respect potential -- Dr. 17 KraH's need to finish his answer. 18 MR. KELLER: Sure. 19 BY MR. KELLER: 20 Q. Who do you recall was a member 21 of the clinical assay sub-teams during the 22 time frame of the development of Protocol 007 23 and the AIGENT? 24 A. I can't say with certainty. I 25 don't recall.</p>	<p style="text-align: right;">Page 269</p> <p>1 Q. Well, did you review minutes as 2 part of your job duties of meetings that you 3 had with CBER? 4 A. I can't say with certainty that 5 I did. 6 Q. So you don't recall whether or 7 not you ever saw those meeting minutes. Is 8 that a fair statement? 9 A. I may have seen them, but I 10 don't recall. They're not looking familiar to 11 me right now. 12 Q. This executive summary that was 13 prepared by Dr. Chirgwin and circulated to 14 Dr. Ukwu and circulated again by Dr. Chirgwin 15 to this laundry list of individuals at Merck, 16 it says under the "Executive Summary," number 17 4 "CBER does not use either complement or IgG 18 to enhance sensitivity and feels that these 19 maneuvers should not be necessary." 20 Do you see that? 21 A. Yes. 22 Q. You don't recall that being 23 discussed at that meeting with CBER, or do 24 you? 25 A. I recall the anti-IgG and</p>

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<p style="text-align: right;">Page 270</p> <p>1 complementing discussed with CBER. Whether it 2 was at this meeting or not, I can't say. 3 Q. Was it something that you 4 proposed to CBER to use in this AIGENT? 5 MR. SANGIAMO: Object to the 6 form. 7 THE WITNESS: As best I can 8 recall, the complement, again, whether 9 it's in the context of this meeting or 10 not, but I -- as best I recall, we had 11 evaluated complement and then provided 12 those data. Or we evaluated complement 13 and saw that it was not usable, meaning 14 that neutralized virus on its own in 15 the absence of serum. 16 BY MR. KELLER: 17 Q. Just so I'm clear -- 18 MR. SANGIAMO: Were you done, 19 Dr. Krah, with your answer? 20 THE WITNESS: The other half to 21 it would be anti-IgG, I remember it 22 being discussed at a meeting with CBER. 23 Whether we proposed it or CBER proposed 24 it, I don't know. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 272</p> <p>1 A. Okay. 2 Q. Could you read what you wrote to 3 Mr. Rubinstein, please? 4 A. I'm sorry, for the Friday, 5 January 17th? 6 Q. Friday, January 17th at 3:25 p.m. 7 A. It says, "Len, Yes - The MMR II 8 Protocol 006 study used a straightforward, 9 non-enhanced neutralization, using several 10 different indicator viruses. The MMR II 11 study...", which it doesn't say here but 12 implies 007, "...used an anti-IgG enhanced 13 neutralization and the low-passaged Jeryl Lynn 14 indicator virus. We would have used the same 15 assay used in 006 and 007...", meaning 16 Protocol 006 and Protocol 007, "...except that 17 we could not achieve the 90 percent 18 seroconversion sensitivity with any of the 19 wild-type mumps strains without enhancing the 20 assay sensitivity. We could measure greater 21 than 90 percent seroconversion using the 22 vaccine strain as the indicator, but CBER 23 required us to use a 'wild-type' indicator 24 virus for 007." 25 Q. Do you recall writing that</p>
<p style="text-align: right;">Page 271</p> <p>1 Q. Fair enough. 2 MR. SANGIAMO: We're an hour and 3 nine minutes out. 4 MR. KELLER: Take a break. 5 VIDEOGRAPHER: The time is now 6 3:17. This concludes disc four. 7 - - - 8 (A recess was taken.) 9 - - - 10 VIDEOGRAPHER: The time is 3:36. 11 This begins disc five. 12 - - - 13 (Exhibit Krah-29, Series of 14 e-mails, 51640 - 51642, was marked for 15 identification.) 16 - - - 17 MR. KELLER: For the record, I'd 18 like to mark as Exhibit 29 a document 19 bearing Bates stamp numbers 51640 to 20 642, which is a series of e-mails. 21 BY MR. KELLER: 22 Q. And, sir, I'd like to direct 23 your attention to the January 17, 2003, e-mail 24 to Leonard Rubinstein on the first page 25 regarding -- do you need any help?</p>	<p style="text-align: right;">Page 273</p> <p>1 e-mail? 2 A. I can't say I recall. It's my 3 writing. I can't say it's my writing, but it 4 sounds like my wording and it's from me so I 5 assume that it -- I don't recall writing it. 6 It's from me in language that I would use. 7 Q. Do you recall that was the 8 reason why Protocol 006, protocol used for 9 Protocol 006 was not used in Protocol 007 10 because you could not achieve the 90 percent 11 seroconversion sensitivity? 12 MR. SANGIAMO: Object to the 13 form. Also, Dr. Krah, if you'd like to 14 review the document in its entirety, 15 please read this. 16 BY MR. KELLER: 17 Q. I'm only asking about this 18 statement. 19 MR. SANGIAMO: Well, it's in 20 context. 21 THE WITNESS: My recollection 22 that the reason for not using one of 23 the viruses, one of the wild type 24 viruses in the Protocol 006 -- the 25 format for Protocol 006 was that we</p>

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<p style="text-align: right;">Page 274</p> <p>1 could not achieve -- and, again, 90 2 percent here seroconversion with that 3 assay format in any of those indicator 4 viruses. 5 BY MR. KELLER: 6 Q. That's why you used Protocol 007 7 in order to reach the targeted greater than 95 8 percent? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: So the AIGENT 12 assay was developed as part of Protocol 13 007 as an assay that was capable of 14 measuring a 95 percent seroconversion. 15 BY MR. KELLER: 16 Q. You couldn't do that with 17 Protocol 006 with a standard PRN assay. 18 Correct? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: Independent of 22 this paragraph, I don't recall what the 23 seroconversion rates were with the 24 different indicator viruses. The way 25 this is worded suggests that the</p>	<p style="text-align: right;">Page 276</p> <p>1 mumps Nt studies. Do you recall drafting this 2 e-mail? 3 A. Again, it's -- I don't recall 4 the specific e-mail, but it's from me in 5 language that I -- looks familiar to me. 6 Q. So is the purpose of this e-mail 7 to update Emini and Shaw and Ms. Yagodich 8 about your developmental activities with 9 regard to the Protocol 007, praecipe that was 10 going to be used for Protocol 007? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: I can't tell at 14 least automatically from this that it 15 was specifically for the purpose of 16 Protocol 007. 17 BY MR. KELLER: 18 Q. Do you see on the last -- on 19 page 2 of your e-mail -- 20 A. Yes. 21 Q. -- it says, We also plan to 22 readdress the use of anti-human IgG to enhance 23 Nt, as a back-up if we fall short of our 90 24 plus percent target. 25 Do you see that?</p>
<p style="text-align: right;">Page 275</p> <p>1 indicator viruses in the Protocol 006, 2 the format of the neutralization assay 3 used for Protocol 006 was not achieving 4 that 90 percent seroconversion rate. 5 BY MR. KELLER: 6 Q. So a decision was made to change 7 that assay with what ultimately became 8 Protocol 007 and the AIGENT. Correct? 9 A. So I would describe it as the 10 AIGENT assay. I wouldn't necessarily link 11 them and say it's Protocol 007 and the AIGENT 12 assay. But it's the AIGENT assay. 13 MR. KELLER: Let me mark this 14 next exhibit as Exhibit 30. 15 - - - 16 (Exhibit Krah-30, 3/30/00 17 E-mail, 336323 - 336325, was marked for 18 identification.) 19 - - - 20 BY MR. KELLER: 21 Q. For the record, Exhibit 30 is a 22 document bear Bates stamp number 336323 23 through 325, and it's an e-mail from you, 24 Dr. Krah, dated March 30, 2000, to Emilio 25 Emini, Alan Shaw, Mary Yagodich, update on</p>	<p style="text-align: right;">Page 277</p> <p>1 A. Yes. 2 Q. Does that lead you to believe 3 that this was, in fact, related to Protocol 4 007? 5 MR. SANGIAMO: Dr. Krah, make 6 sure you've aptly read the e-mail 7 before you respond to questions. 8 BY MR. KELLER: 9 Q. Do you see it specifically calls 10 out the 007 study? 11 A. Some of the variables that we 12 were looking at are ones that are familiar to 13 me from discussions with CBER as part of the 14 discussions about Protocol 007. But I don't 15 see here that it specifically identifies it as 16 part of the Protocol 007 assay development. 17 Q. The part you're referring to is 18 the use of immunostaining? 19 A. I think the -- well, immunostaining 20 was part of it. The Spearman-Karber method. 21 The part that I was regarding as the Barnes 22 strain on page 2, the reference to the Barnes 23 strain from Dr. Forghani. As best I recall, 24 that was included as part of some of the 25 discussion with CBER, suggestion to consider</p>

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<p style="text-align: right;">Page 278</p> <p>1 that strain.</p> <p>2 Q. For Protocol 007. Correct?</p> <p>3 A. Yes.</p> <p>4 Q. And the low passage Jeryl Lynn,</p> <p>5 JL135, that was what was used in Protocol 007,</p> <p>6 wasn't it?</p> <p>7 A. Yes.</p> <p>8 Q. So the antihuman IgG was also</p> <p>9 used in Protocol 007. Correct?</p> <p>10 A. Yes.</p> <p>11 Q. So I'm confused by your answer</p> <p>12 why you don't think this was a discussion</p> <p>13 about updating about your efforts to develop</p> <p>14 an assay for Protocol 007. Many of the things</p> <p>15 discussed were discussed about updating Emini</p> <p>16 and Shaw and Yagodich about your efforts to</p> <p>17 come up with a methodology to find an answer</p> <p>18 that would get you to 95 percent seroconversion.</p> <p>19 Correct?</p> <p>20 A. Yes.</p> <p>21 MR. SANGIAMO: Object to the</p> <p>22 form. Misstates his testimony.</p> <p>23 BY MR. KELLER:</p> <p>24 Q. Here when you say we also plan</p> <p>25 to readdress the use antihuman IgG to enhance</p>	<p style="text-align: right;">Page 280</p> <p>1 being more consistent with what CBER</p> <p>2 had experienced within their testing.</p> <p>3 BY MR. KELLER:</p> <p>4 Q. And so you saw a memo from CBER</p> <p>5 saying that they didn't think that step was</p> <p>6 necessary. So was that one of the reasons why</p> <p>7 you considered it as only a backup plan if you</p> <p>8 couldn't get any other methods to get you to</p> <p>9 reach the 95 percent seroconversion target?</p> <p>10 A. I can't say with certainty what</p> <p>11 the thought process was at the time, but</p> <p>12 looking back on it, if they thought it wasn't</p> <p>13 necessary, I would -- if I were doing this</p> <p>14 today, would try it without and then if it</p> <p>15 wasn't successful, then go with the anti-IgG.</p> <p>16 Q. Do you recall any discussions at</p> <p>17 Merck about concerns with the use of this IgG</p> <p>18 maneuver?</p> <p>19 MR. SANGIAMO: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: Not that I recall.</p> <p>22 BY MR. KELLER:</p> <p>23 Q. Nobody voiced any criticism</p> <p>24 about using the IgG maneuver --</p> <p>25 MR. SANGIAMO: Object to the</p>
<p style="text-align: right;">Page 279</p> <p>1 Nt. Nt, that's neutralizing. Right?</p> <p>2 A. Neutralization, yes.</p> <p>3 Q. Neutralization. As a backup</p> <p>4 plan if we fall short of the 90 percent plus</p> <p>5 target.</p> <p>6 Why was it a backup plan?</p> <p>7 A. I can't say with certainty, but</p> <p>8 my best recollection is that we were --</p> <p>9 from -- that we would see if we could achieve</p> <p>10 a 90 percent seroconversion without adding the</p> <p>11 IgG and then if it wasn't achievable, evaluate</p> <p>12 addition of that as a CBER suggestion to</p> <p>13 increase the neutralization sensitivity.</p> <p>14 Q. And so -- I'm confused. I</p> <p>15 apologize if I'm confused. But let me ask you</p> <p>16 to rectify my confusion. Strike that.</p> <p>17 Why was using anti-IgG something</p> <p>18 that was a backup plan and not used up front?</p> <p>19 MR. SANGIAMO: Object to the</p> <p>20 form.</p> <p>21 THE WITNESS: My best recollection</p> <p>22 is that we were trying to -- our</p> <p>23 minimizing steps in the assay,</p> <p>24 minimizing reagents that are needed</p> <p>25 more for assay simplicity and also are</p>	<p style="text-align: right;">Page 281</p> <p>1 form.</p> <p>2 BY MR. KELLER:</p> <p>3 Q. -- in this assay in Protocol</p> <p>4 007?</p> <p>5 MR. SANGIAMO: Object to the</p> <p>6 form.</p> <p>7 THE WITNESS: No. And, in fact,</p> <p>8 the assay was based on a publication</p> <p>9 that CBER had published.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. Back in 19 -- early 1970s.</p> <p>12 Correct?</p> <p>13 A. Yes.</p> <p>14 Q. That was before even ELISA</p> <p>15 assays had become standard practice in the</p> <p>16 industry. Correct?</p> <p>17 A. That, I can't --</p> <p>18 Q. You don't know?</p> <p>19 A. I don't know.</p> <p>20 Q. Are you aware of any other --</p> <p>21 have you ever used the rabbit anti-IgG step</p> <p>22 after Protocol 007?</p> <p>23 A. Me personally?</p> <p>24 Q. Yes.</p> <p>25 A. There are some discussions I've</p>

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<p style="text-align: right;">Page 282</p> <p>1 had with others -- I don't recall using it 2 personally, but discussions with other 3 colleagues that I've had of potentially using 4 it. 5 Q. What colleagues did you discuss 6 it with? 7 A. I recall some colleagues in MMD 8 who were trying to identify means, as best I 9 can recall, means to increase the 10 neutralization capacity of a serum in a 11 tissue -- I think what was called a tissue 12 culture safety test. And one option that I 13 proposed was adding anti-IgG. 14 Q. Was that a -- was that test at 15 all linked to protection? 16 A. No. 17 Q. Do you recall ever -- at any of 18 these CAS meetings you had, nobody voiced any 19 concern about nonspecific neutralization as a 20 result of using rabbit anti-IgG step? 21 MR. SANGIAMO: Object to the 22 form. 23 THE WITNESS: I don't recall any 24 objections. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 284</p> <p>1 Q. Do you recall presenting the use 2 of the anti-IgG at a CAS subcommittee meeting 3 or a Clinical Assay Subcommittee Meeting? 4 A. I recall presenting the data. I 5 don't recall the specific meeting. 6 MR. KELLER: For the record, 7 Exhibit 31 is an agenda, looks like 8 there's a typo on the title of this, it 9 says, "CRITICAL ASSAY SUBCOMMITTEE 10 MEETING." 11 BY MR. KELLER: 12 Q. You understand it to be 13 clinical, correct, October 24, 2000? 14 MR. SANGIAMO: Objection. 15 THE WITNESS: I can't -- I don't 16 know. 17 BY MR. KELLER: 18 Q. Under "TEAM PRESENTATION," it 19 says -- identifies you, Dr. Krah to present on 20 the enhanced mumps neutralization assay. Do 21 you see that? 22 A. Yes. 23 Q. That's the AIGENT. Correct? 24 A. That's my enhanced mumps -- 25 mumps neutralization assay is what I refer to</p>
<p style="text-align: right;">Page 283</p> <p>1 Q. Did Dr. Sadoff ever object? 2 A. I don't recall. 3 Q. Do you ever recall discussing 4 the use of the anti-IgG maneuver with 5 Dr. Sadoff? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: That, I don't 9 recall. 10 BY MR. KELLER: 11 Q. What about Dr. Musey? 12 A. I recall discussing the assay 13 with him, but as far as discussing anti-IgG, I 14 don't recall. 15 Q. Do you recall discussing the 16 step with Dr. Thaler? 17 A. That, I don't recall. 18 MR. KELLER: Mark this next 19 exhibit as Exhibit 31. 20 - - - 21 (Exhibit Krah-31, Subcommittee 22 meeting agenda, 2142149, was marked for 23 identification.) 24 - - - 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 285</p> <p>1 as the AIGENT assay, and I would expect that 2 that's what they're referring to here. 3 Q. Here it says, "Update on 4 performance of the assay." 5 Do you see that? 6 A. Yes. 7 Q. Do you recall updating the CAS 8 on the performance of the AIGENT? 9 A. I remember presentations on the 10 assay. I don't remember this particular 11 meeting what was covered. 12 Q. It says at the invitees, 13 Dr. Thaler was there. Do you see that? 14 A. Yes. 15 Q. Mary Yagodich? 16 A. Yes. 17 Q. Dr. Chirgwin? 18 A. Yes. 19 Q. What was William Long's role in 20 Protocol 007? He was invited as well. 21 Correct? 22 A. Yes. His name is on here. He 23 wasn't in the same department as I was, and I 24 don't recall what his specific -- what his 25 role was.</p>

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<p style="text-align: right;">Page 286</p> <p>1 Q. Did he also run clinical 2 study -- strike that. 3 Did he also run any experiments 4 with the PRN assay -- 5 MR. SANGIAMO: Object to the 6 form. 7 BY MR. KELLER: 8 Q. -- in developing Protocol 007, 9 do you know? 10 MR. SANGIAMO: Object to the 11 form. 12 THE WITNESS: I am aware of, as 13 best I can recall, a CPE-based assay 14 that he was working on, not a plaque 15 reduction, to my knowledge. 16 - - - 17 (Exhibit Krah-32, Anti-IgG 18 Enhanced Mumps Neutralizing 19 Assay-Update: October 24, 2000, 26912 20 - 26918, was marked for identification.) 21 - - - 22 MR. KELLER: For the record, 23 Exhibit 32 is a document that bears 24 Bates stamp numbers 26912 through 918, 25 entitled: Anti-IgG Enhanced Mumps</p>	<p style="text-align: right;">Page 288</p> <p>1 wording. I can't exclude that someone didn't 2 contribute to it, but at least the majority of 3 the wording looks like it's my wording. 4 Q. In the experiments that 5 supported this particular document -- did you 6 provide this copy to the CAS subcommittee or 7 was it just a presentation -- strike that. 8 Did you provide a copy of 9 Exhibit 32 to the CAS subcommittee? 10 A. I don't recall. 11 Q. And the individuals on 12 Exhibit 31, D. Arena, Dr. Chirgwin, William 13 Long, S. Olsen, N. Morsy, J. Staub, Dr. Thaler 14 and Ms. Yagodich, were those members of the 15 CAS? 16 A. I can't say for certain. 17 Q. And if you look on the first 18 page of 269123 of Exhibit 32, can you read the 19 objective that you wrote? 20 MR. SANGIAMO: Object to the 21 form. 22 THE WITNESS: The objective, as 23 listed, is "Identify a mumps 24 neutralization assay format using a 25 'wild-type' mumps strain that permits</p>
<p style="text-align: right;">Page 287</p> <p>1 Neutralizing Assay-Update: October 24. 2 BY MR. KELLER: 3 Q. Do you see that? 4 A. I'm sorry, repeat the last part 5 of that? 6 Q. I'm just reading the title. Do 7 you see the title? 8 A. Anti-IgG enhanced, okay, yes. 9 Q. So is this the presentation that 10 you gave to the CAS subcommittee on October 24? 11 A. It's the same date, but I don't 12 have an immediate recollection of the 13 presentation, but that's the date, the same 14 date as the clinical assay sub-committee 15 meeting. 16 Q. Do you have any reason to 17 believe that you didn't present it on that 18 date? 19 A. No. If it's dated, I would 20 expect -- my expectation would be if it's 21 dated that date, that that's the date it was 22 provided. 23 Q. Did you draft this document, 24 Exhibit 32? 25 A. The wording looks like my</p>	<p style="text-align: right;">Page 289</p> <p>1 measurement of a 95 percent 2 seroconversion rate in MMR II 3 vaccinees." 4 BY MR. KELLER: 5 Q. Is that the objective you used 6 to develop the AIGENT? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: The AIGENT 10 assay -- development of the AIGENT 11 assay was to determine if we could 12 develop an assay that was capable of 13 measuring 95 percent seroconversion. 14 So it's consistent with that. 15 BY MR. KELLER: 16 Q. In fact, you did develop the 17 AIGENT that resulted in -- strike that. 18 Did the -- strike that. 19 If you look on the next page, 20 29 -- I'm sorry, 26913, it says, "Data 21 presented at the August 18, 2000 CAS meeting." 22 Do you see that? 23 A. Yes. 24 Q. Do you recall presenting this 25 data to the Clinical Assay Subcommittee?</p>

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<p style="text-align: right;">Page 290</p> <p>1 A. I do not. 2 MR. SANGIAMO: Object to the 3 form. 4 BY MR. KELLER: 5 Q. Any reason you didn't if that's 6 what it says? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: If that's what it 10 says, I have no contrary evidence that 11 I didn't. 12 BY MR. KELLER: 13 Q. Just so I understand, it says, 14 Evaluation of seroconversion rates achievable 15 in the Anti-IgG Enhanced Nt - results from 16 subset of Protocol 006 and another set of 60 17 paired PRN assay. 18 Do you see that? 19 A. Yes. 20 Q. So did you use the samples from 21 Protocol 006 to develop Protocol 007? 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: The wording of 25 this suggests that those were a subset</p>	<p style="text-align: right;">Page 292</p> <p>1 Q. So you took -- you have 2 conversion rates for this set. So you're 3 retesting the same kids in three different 4 experiments to see how those kids respond. 5 Correct? Is that fair to say? 6 A. No. I'm sorry, you're referring 7 to the seroconversion rate? 8 Q. You got three -- under 9 "Seroconversion rates for this set," it says 10 Jeryl Lynn "standard" Nt: 31 out of 39, 11 79.5 percent. JL135 at 1 to 4 anti-IgG 33 out 12 of 36 equals 91.7 percent. Jeryl at 1 to 8 13 anti-IgG neutralizing 32 to 34, 94 percent. 14 Do you see that? 15 A. Yes. 16 Q. Were they -- these the same kids 17 or different kids? 18 A. I'm sorry, different kids from 19 what? 20 Q. I'm asking you, are these 21 retesting the same kids or are you just -- 22 A. I'm sorry. Okay. My best 23 recollection is that they're the same kids 24 tested in three different -- let's start -- I 25 can't say with certainty from this. I have an</p>
<p style="text-align: right;">Page 291</p> <p>1 of sera for Protocol 006 and additional 2 sera were included in the evaluation 3 that's listed here. 4 BY MR. KELLER: 5 Q. So explain to me serum set 6 number one. It says, "Subset of sera from 7 Protocol 006 (includes set of 12 sera biased 8 toward non-responders to Jeryl Lynn by 9 'standard' Nt)." 10 Do you see that? 11 A. Yes. 12 Q. Standard Nt, is that the PRN 13 assay that was run in Protocol 006? Were you 14 following that protocol? 15 A. That -- 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: I can't say with 19 certainty. My expectation is that they 20 would have had to have been tested at 21 some point. And Protocol 006 wouldn't 22 have been the opportunity. I can't say 23 with certainty that that's where they 24 were tested. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 293</p> <p>1 expectation for it, but I can't say the way 2 this is worded, I can't say with 100 percent 3 certainty that they're the same kids tested 4 under three different conditions. 5 Q. But that's what it looks like 6 from the face of it. Correct? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: That's -- my 10 expectation looking back at it would be 11 that they're the same sera tests at 12 three different formats, but I can't 13 say with 100 percent certainty today. 14 BY MR. KELLER: 15 Q. And so if -- okay. Fair enough. 16 Let me direct your attention to 17 the next page, 26915. It says, conclusion 18 from previous testing of 1 to 4 anti-IgG -- 19 I'm sorry, two pages over. 26915. I 20 apologize. Here you write, Measurement of 21 greater than 95 percent seroconversion in 22 vaccinees is achievable. 23 Do you see that? 24 A. Yes. 25 Q. That's what your experiments</p>

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<p style="text-align: right;">Page 294</p> <p>1 showed, correct, with the use of anti-IgG 2 maneuver? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: For serum set one, 6 no. Serum set two on the page just 7 before has a 96 percent seroconversion 8 rate including anti-IgG. So there was 9 a condition for one of the two -- one 10 of the serum panels that one is 11 achieving a 95 percent seroconversion. 12 BY MR. KELLER: 13 Q. So the standard panel only got 14 you 79.5 percent. But with using different 15 dilutions of anti-IgG, you can get that up to 16 96 percent. Correct? 17 MR. SANGIAMO: Object to the 18 form. 19 THE WITNESS: At least in serum 20 set one we had approximately an 21 80 percent seroconversion rate without 22 the anti-IgG. What I can't tell from 23 the wording here is if that is -- 24 refers to JL135 for the anti-IgG part. 25 So what I'm not able to say with</p>	<p style="text-align: right;">Page 296</p> <p>1 desirable number was set, I don't recall. 2 Q. I see. The third bullet point 3 you say, Continue evaluation of results using 4 optimized anti-IgG (target less than equal 10 5 percent pre-positive rate and greater than/ 6 equal to 95 percent seroconversion). 7 Do you see that? 8 A. Yes. 9 Q. Where did you come up with that 10 10 percent pre-positive rate? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: I don't recall 14 where that came from. 15 BY MR. KELLER: 16 Q. So at this point you were still 17 developing the assay to try to reach that 18 target. Correct? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: My recollection is 22 that we were still developing the assay 23 to see if we could achieve 95 percent 24 seroconversion. 25 BY MR. KELLER:</p>
<p style="text-align: right;">Page 295</p> <p>1 certainty is the contribution of the 2 wild -- of the low passage Jeryl Lynn 3 and the anti-IgG. By using the 4 combination of low passage Jeryl Lynn 5 and anti-IgG, we were able to get 6 96 percent seroconversion. 7 BY MR. KELLER: 8 Q. Did you ever do any experiments 9 running the standard PRN assay with Jeryl Lynn 10 135 without the anti-IgG maneuver? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: I don't recall 14 with certainty. I have an expectation 15 of it, but I don't recall with 16 certainty. 17 BY MR. KELLER: 18 Q. 26915, second bullet point you 19 say, "Pre-positive rate is higher than 20 desirable." What did you mean by that when 21 you wrote that? 22 A. My best recollection based on 23 the description for serum set two was that the 24 value was 22 percent, and that that was higher 25 than what was deemed desirable. How that</p>	<p style="text-align: right;">Page 297</p> <p>1 Q. Was one of the collateral 2 problems of using the anti-IgG step is a 3 higher pre-positive rate than you would expect 4 in the real world? 5 A. What we did observe is an 6 increase -- page 26916 is an example of that, 7 using different levels of anti-IgG can give 8 varying levels of pre-positivity rate. As far 9 as what the pre-positivity rate in the real 10 world is, I can't speak to what that is. 11 Q. I showed you the protocol from 12 February of 1999 that expected -- said it 13 expected a 5 percent pre-positive rate. Do 14 you recall any discussion about the difference 15 between the original 5 percent expectation and 16 your 10 percent expectation? 17 MR. SANGIAMO: Object to the 18 preamble. You can answer the question. 19 THE WITNESS: Not that I recall. 20 BY MR. KELLER: 21 Q. Did that higher than desirable 22 pre-positive rate continue through when you 23 ran the serums in Protocol 007? 24 MR. SANGIAMO: Object to the 25 form.</p>

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<p style="text-align: right;">Page 298</p> <p>1 THE WITNESS: I don't recall 2 what the pre-positive rate was for the 3 Protocol 007 set. 4 BY MR. KELLER: 5 Q. Were you focused on 6 pre-positives when you were running the serums 7 for Protocol 007? 8 MR. SANGIAMO: Object to the 9 form. 10 THE WITNESS: We were not 11 focused on the pre-positive. 12 BY MR. KELLER: 13 Q. You didn't care whether or not 14 it was pre-positive or not, is that your 15 testimony? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: My testimony is 19 that we -- if we did have a 20 pre-positive, that we were interested 21 to make sure that it was an accurate 22 representation of a plaque number. 23 BY MR. KELLER: 24 Q. How did you do that? 25 A. One way in which it was checked</p>	<p style="text-align: right;">Page 300</p> <p>1 positive, it would be -- the post -- it 2 depends on the post-vaccination serum 3 result, meaning that if a 4 pre-vaccination serum was positive 5 single dilution, and then 6 post-vaccination serum had an invalid 7 result, that pre-vaccination serum will 8 be tested not because it's a 9 pre-vaccination positive. 10 BY MR. KELLER: 11 Q. So you didn't retest valid 12 assays in Protocol 007 that had a valid -- 13 that had a pre-positive at one dilution to see 14 whether or not you could -- it would switch to 15 a pre-negative? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: There were cases I 19 recall where we did have some samples 20 that included examples such as a 21 positive single -- pre-vaccination 22 serum that was positive single dilution 23 that were retested with the intent of 24 trying to verify whether the result was 25 confirmed.</p>
<p style="text-align: right;">Page 299</p> <p>1 would be to look at the plaque counts that 2 were recorded for, in some cases, pre-positives 3 but in other cases, specific situations, for 4 example, single pre- -- not pre-positive, but 5 single positive dilution and a number of other 6 I'll say unexpected neutralization results and 7 have either the original counter or other 8 counter look at the plaques and see if plaques 9 were being miscounted. 10 Q. Did you do that for the 11 post-vaccination positives? 12 A. Yes. 13 Q. For both? 14 A. For the single positive 15 dilution, yes. 16 Q. So you didn't see from your 17 development of Protocol 007 that if you 18 retested -- I'm sorry. 19 Did you ever retest 20 pre-positives out of a single dilution? 21 MR. SANGIAMO: Object to the 22 form. 23 THE WITNESS: As best I can 24 recall, if a pre-positive -- positive 25 single dilution was confirmed to be</p>	<p style="text-align: right;">Page 301</p> <p>1 BY MR. KELLER: 2 Q. So when you were running the 3 protocol samples, you could tell what is a 4 pre-vaccination sample and a post-vaccination 5 sample. Right? 6 A. Yes. 7 Q. Let me move on to the document 8 26917. Here it says, "Proposal for Testing a 9 Subset of Samples from the End-Expiry Study." 10 Do you see that? 11 A. Yes. 12 Q. At a certain point there was a 13 decision made that a subset analysis would be 14 run. Correct? 15 A. Using the AIGENT assay, yes. 16 Q. Do you recall what precipitated 17 that decision? 18 A. I do not require -- I do not 19 recall the specific event that triggered it. 20 Q. Do you recall general discussion 21 with Emilio Emini where they discussed an 22 emergency that was going on? 23 A. Yes. 24 Q. What was that emergency? 25 A. I don't recall him telling me.</p>

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1 Q. He didn't tell you that there
 2 was a 483 that was issued out of MMD based on
 3 an FDA inspection with stability problems in
 4 the MMR product?
 5 A. I recall that a warning letter
 6 was issued. What that contained or involved,
 7 I don't have a recollection.
 8 Q. Do you recall a 483 that came
 9 before the warning letter?
 10 A. I do not.
 11 Q. Back to 26917, the second bullet
 12 point says, "Validation runs concurrent with
 13 clinical serum testing."
 14 Do you see that?
 15 A. Yes.
 16 Q. Henrietta Ukwu had sent an
 17 e-mail earlier saying that do not run -- do
 18 not run the validation concurrent with testing
 19 the serum but finish the validation and then
 20 test the serum. Do you recall that e-mail?
 21 MR. SANGIAMO: Object to the
 22 characterization of the e-mail.
 23 THE WITNESS: I recall the
 24 e-mail that you showed me previously
 25 suggesting that the validation be done

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1 before the clinical testing starts.
 2 BY MR. KELLER:
 3 Q. Here it says validation runs
 4 concurrent with clinical serum testing. You
 5 understand that what they're saying is
 6 validate the AIGENT assay at the same time
 7 that you're running the clinical samples?
 8 A. Yes. And that was done in
 9 collaboration with CBER. They were informed
 10 that that was being done and approved that
 11 approach.
 12 Q. When did they approve that
 13 approach? Were you at a meeting when that was
 14 approved?
 15 MR. SANGIAMO: Object to the
 16 form.
 17 THE WITNESS: I don't recall if
 18 I was at a -- with certainty that I was
 19 at that meeting.
 20 BY MR. KELLER:
 21 Q. Were you at that meeting or not?
 22 A. I don't recall.
 23 Q. So you remember, you recall who
 24 told you -- who do you recall telling you that
 25 CBER approved running the validation

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1 experiments for the AIGENT SOP at the same
 2 time or concurrently with running the clinical
 3 serum in the assay for Protocol 007?
 4 A. I don't recall who --
 5 Q. How do you know that?
 6 MR. SANGIAMO: Whoa, whoa.
 7 Jeff, you have to let him finish his
 8 answer.
 9 MR. KELLER: Sure.
 10 MR. SANGIAMO: By the way, I
 11 object because it's asked and answered.
 12 THE WITNESS: My recollection of
 13 how I know that is that the -- someone
 14 in authority at Merck indicated that we
 15 would do the validation study in
 16 parallel -- not necessarily in
 17 parallel, but before the clinical
 18 testing -- sorry. We would start
 19 Protocol 007 testing for the interim,
 20 the subset analysis before completing
 21 the validation studies.
 22 BY MR. KELLER:
 23 Q. Did they tell you why?
 24 A. I don't recall them telling me
 25 why.

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1 Q. That's what you did, isn't it,
 2 you ran the clinical samples while you were
 3 validating the SOP? Correct?
 4 MR. SANGIAMO: Object to the
 5 form.
 6 THE WITNESS: We did, but I
 7 recall from the CBER discussion when we
 8 indicated we would be running the
 9 subset analysis, or the validation and
 10 parallel to subset analysis, that the
 11 assay would not change. So the
 12 validation would be characterizing the
 13 assay and the results of the validation
 14 study would be applied before the
 15 results of the subset analysis were
 16 reported.
 17 BY MR. KELLER:
 18 Q. What communication -- when was
 19 this? Was this before you started running the
 20 assays or after?
 21 MR. SANGIAMO: Object to the
 22 form.
 23 THE WITNESS: I can't say I
 24 recall with certainty when that was
 25 communicated.

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<p style="text-align: right;">Page 306</p> <p>1 BY MR. KELLER: 2 Q. Is that -- was that a meeting 3 that you were at that CBER approved of you 4 running the clinical samples for Protocol 007 5 before you validated the assay? 6 A. I can't say with certainty that 7 I was at the meeting, but my recollection is 8 that there was an agreement that we were not 9 changing the assay so running the -- doing the 10 validation concurrently with testing of 11 Protocol 007 was acceptable to them. 12 Q. But you weren't at that meeting, 13 that's just somebody at Merck told you that? 14 A. I may have been at the meeting. 15 I don't recall with certainty if I was or 16 wasn't. 17 Q. Was that written down anywhere? 18 MR. SANGIAMO: Objection. Calls 19 for speculation. 20 THE WITNESS: I don't recall if 21 it was or wasn't. 22 BY MR. KELLER: 23 Q. I see. Have you ever run a 24 clinical study before Protocol 007? 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 308</p> <p>1 Do you see that? 2 A. Yes. 3 Q. Does that refresh your memory 4 that you were working with Joe Antonello from 5 biologics research? 6 A. Biometrics. 7 Q. Biometrics research? 8 A. I recall he was one of the 9 people from that group who we were talking to 10 in developing the validation plan or protocol. 11 Q. So did you -- you drafted the 12 validation protocol. Correct? 13 MR. SANGIAMO: Objection. Asked 14 and answered. Misstates testimony. 15 BY MR. KELLER: 16 Q. You don't recall? 17 A. I don't -- I don't recall who 18 drafted it. 19 Q. And here, if you look at this 20 discussion, do you recall discussing -- you 21 can feel free to read the reference on 22 October 27 to your communications with Joe 23 Antonello. Do you recall discussing the 24 parameters of what that protocol would look 25 like?</p>
<p style="text-align: right;">Page 307</p> <p>1 form. 2 THE WITNESS: I have -- I and my 3 group have run assays in support of 4 clinical -- at least one other clinical 5 study. 6 BY MR. KELLER: 7 Q. That clinical study, is that 8 Protocol 006? 9 A. Yes. 10 Q. Did you validate that assay 11 before you ran the serum in Protocol 006? 12 A. There were some validation 13 experiments, as best I can recall, that were 14 done before starting that testing. I don't 15 recall if the validation was completed for all 16 the viruses before the Protocol 006 testing 17 started. 18 Q. If you could go back to your 19 journal for 2000. If I could direct your 20 attention to October 27, at 490473 or 393 of 21 your journal. 22 A. 490473. 23 Q. There's a reference here to a 24 meeting with Joe Antonello at 9:00 a.m. to 25 review validation protocol for mumps AIGENT.</p>	<p style="text-align: right;">Page 309</p> <p>1 A. So at least the points I have 2 listed here I wouldn't say it's all inclusive 3 of all the points that were discussed, but 4 these are some examples of aspects of the 5 validation that he was suggesting. 6 Q. If you look at one, two, three, 7 four down, it talks about specificity. Do you 8 see that? 9 A. Yes. 10 Q. Can you read that line from your 11 journal? 12 A. Yeah. Specificity can be 13 addressed from pre/post boost and absorption 14 experiment. 15 Q. So did you understand that what 16 that pre/post boost was, do you recall any 17 discussion about what that experiment would 18 be? 19 MR. SANGIAMO: Object to the 20 form. You're asking if he recalls any 21 discussion of it? 22 MR. KELLER: Yes. 23 THE WITNESS: I don't. 24 MR. SANGIAMO: That's different 25 from the first question you asked.</p>

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<p style="text-align: right;">Page 310</p> <p>1 That's why I asked for clarification. 2 THE WITNESS: I don't recall 3 there being discussion over what he 4 meant by that. 5 BY MR. KELLER: 6 Q. So you don't know what a 7 pre/post boost experiment would be for 8 specificity? 9 A. I am familiar not from mumps or 10 -- from other literature that I'm familiar 11 with, of studies in which that has been looked 12 at, but it requires -- at least ones I'm 13 familiar with requires a monovalent 14 vaccination. Meaning mumps, mumps alone not 15 in the context of MMR. 16 Q. Did you ever consider running 17 that experiment as part of your validation of 18 the AIGENT? 19 A. As best I understand or can 20 recall, we didn't include that. I can't say 21 that we -- I don't recall if we considered it 22 or not. 23 MR. KELLER: Let me mark -- let 24 me mark this next exhibit as Exhibit 33. 25 - - -</p>	<p style="text-align: right;">Page 312</p> <p>1 Q. Sorry. The earlier e-mails 2 start in -- 3 A. Yeah. Yes. Okay. 4 Q. Here the subject was, Validation 5 protocol for anti-IgG enhanced mumps neut 6 assay. Do you see that? 7 A. Yes. 8 Q. That's Protocol 007. Correct? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: That's the 12 neutralization assay that was used in 13 Protocol 007. 14 BY MR. KELLER: 15 Q. That's the AIGENT. Correct? 16 A. The AIGENT assay, yes. 17 Q. Here you say, The following are 18 some thoughts on the validation protocol for 19 the mumps neut assay to be transferred to Dick 20 Ward's lab -- Dick Ward's group. Do you see 21 that? 22 A. Yes. 23 Q. It says, "I am providing these 24 to get the ball rolling on developing the 25 validation protocol."</p>
<p style="text-align: right;">Page 311</p> <p>1 (Exhibit Krah-33, Series of 2 e-mails with attachment, 759836 - 3 759847, was marked for identification.) 4 - - - 5 MR. KELLER: For the record, 6 Exhibit 33 is a document that bears 7 Bates stamp numbers 79 -- 759836 8 through 847. It's a series of e-mails 9 and an attachment of a validation 10 protocol. 11 BY MR. KELLER: 12 Q. Can you tell me -- can you take 13 a minute to look at this document and see if 14 you recall receiving these e-mails and writing 15 these e-mails that are identified in 16 Exhibit 33. Let me know when you're done. 17 A. Okay. 18 Q. Let me direct your attention to 19 79 -- sorry, 759837, which is your e-mail of 20 October 10, 2000, to Dr. Schofield, amongst 21 another -- Joe Antonello, William Long, 22 Michael Washabaugh. Do you see that? 23 A. I'm sorry? 24 Q. The bottom. 25 A. Oh, okay. Okay. Yes.</p>	<p style="text-align: right;">Page 313</p> <p>1 Do you see that? 2 A. Yes. 3 Q. So you were involved in 4 developing the validation protocol. Correct? 5 A. I was involved in it. What my 6 specific role was, I can't say for sure. 7 Q. Was the purpose -- was the idea 8 as -- back in October 10th, that the 9 validation would be -- the validation analysis 10 and experiments would happen at Dick Ward's 11 lab? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: That, I don't 15 recall. 16 BY MR. KELLER: 17 Q. That appears to be what you said 18 in this e-mail, though. Correct? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: It comments on 22 validation protocols for the assay to 23 be transferred to Dick Ward's group. I 24 don't read it to mean whose -- whether 25 validation would be done at Dick Ward's</p>

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<p style="text-align: right;">Page 314</p> <p>1 lab or at Merck. Validation protocol 2 would be prior to the potential 3 transfer to Dick Ward's lab. 4 BY MR. KELLER: 5 Q. So as of October 30, the 6 decision was made to run that 600 subset out 7 of your lab. Correct? 8 MR. SANGIAMO: Object to the 9 form. 10 THE WITNESS: The date? 11 BY MR. KELLER: 12 Q. As of October 30, after the 13 October meeting with the CAS, do you recall 14 having discussion with Emilio Emini where you 15 were informed that you would run the subset 16 out of your lab? 17 A. I recall being informed by 18 Emilio that our lab will be running the 19 subset. I don't recall the date, the specific 20 date. 21 Q. Fair enough. Here on 22 October 30, on the first page of Exhibit 33, 23 there's an e-mail from Joe Antonello to you, 24 Dr. Krah. Do you see that? 25 A. Yes.</p>	<p style="text-align: right;">Page 316</p> <p>1 samples have already been tested, the 2 remaining samples can be divided among six 3 runs used to assess precision). 4 Do you see that? 5 A. Yes. 6 Q. Then it says, "The test sample 7 data will be used to establish a 8 'sero-positivity' cutoff and provide estimates 9 of pre- and post-vaccination sero-positive 10 rates." 11 Do you see that? 12 A. Yes. 13 Q. This 100 pediatric sample, that 14 was the proposal by Joseph Antonello. Correct? 15 MR. SANGIAMO: Object to the 16 form. 17 BY MR. KELLER: 18 Q. For the validation protocol? Is 19 that a fair statement? 20 MR. SANGIAMO: Object to the 21 form. 22 THE WITNESS: That -- according 23 to the way this is written, that's his 24 recommendation for the serostatus 25 cutoff part of the validation protocol.</p>
<p style="text-align: right;">Page 315</p> <p>1 Q. Again, it's, Validation of 2 protocol for the anti-IgG enhanced mumps neut 3 assay. 4 Do you see that? 5 A. Yes. 6 Q. It says, "Dave, To help in 7 preparing a Mumps PRN Validation Protocol, two 8 recently completed validation protocols are 9 attached." 10 Do you see that? 11 A. Yes. 12 Q. So does that lead you to believe 13 that you were, again, helping prepare that 14 validation protocol or refresh your memory to 15 that effect? 16 A. To my understanding, reinforces 17 that I was involved in trying to identify 18 conditions for the validation protocol. It 19 doesn't clarify to me who the author would be. 20 Q. Fair enough. So in the second, 21 third paragraph under "Sero-Status Cutoff 22 (information on Pre- and Post-Vaccination 23 Rates)," Joseph Antonello writes, Test around 24 100 pediatric pre- and post-vaccination 25 samples (since approximately half of these</p>	<p style="text-align: right;">Page 317</p> <p>1 BY MR. KELLER: 2 Q. That's part of the mock control 3 limits as well. Correct? 4 MR. SANGIAMO: Object to the 5 form. 6 BY MR. KELLER: 7 Q. Is that how you calculate the 8 mock control units? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: I don't believe 12 so. The mock -- my understanding of 13 the mock control, it's a no serum 14 control. So it's virus, control 15 medium, anti-IgG that has limits that 16 are set that are, my understanding, not 17 related to the serostatus cutoff. 18 BY MR. KELLER: 19 Q. So seropositivity, that's -- how 20 would these 100 pediatric pre- and 21 post-vaccine samples be used to set the 22 seropositivity cutoff? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: I don't recall how</p>

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<p style="text-align: right;">Page 318</p> <p>1 it would be applied. I can say that 2 he's suggesting that that number of 3 samples would be recommended to allow 4 him to do that part of his analysis. 5 But beyond that, I don't have any 6 information. 7 BY MR. KELLER: 8 Q. You're not -- you don't know how 9 the sero classification cutoffs are generated, 10 that's for the statisticians? 11 A. The statisticians -- my 12 understanding of the process is that the 13 statisticians confirm what serostatus cutoff 14 is appropriate. So we'll have data, meaning 15 percent of mock and a titer, the statistician 16 then would be able to, through the validation 17 protocol, evaluate what's a statistically 18 supported cutoff. 19 Q. So this mock control, you 20 testified that it's control medium, IgG, and 21 virus. Correct? 22 A. Yes. 23 Q. What was the purpose of having 24 the control medium? 25 A. The -- my -- it doesn't just</p>	<p style="text-align: right;">Page 320</p> <p>1 MR. SANGIAMO: Object to the 2 form. 3 BY MR. KELLER: 4 Q. A handful of kids, like four 5 kids in there? 6 MR. SANGIAMO: Object to the 7 form. 8 BY MR. KELLER: 9 Q. Do you recall? 10 A. I don't recall the number of 11 kids, but the mock serum control is not -- are 12 not related to the performance of the -- the 13 question about whether anti-IgG is 14 neutralizing on its own or not is not relevant 15 to that assay. 16 Q. Did you see any effect of -- you 17 said you ran these assays to say that there 18 was no effect with or without the anti-IgG? 19 A. In the absence of serum. 20 Q. But in the absence of serum 21 there's a huge effect. Correct? 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: It depends on the 25 serum. It depends on the serum.</p>
<p style="text-align: right;">Page 319</p> <p>1 apply to this assay but other assays. My 2 objective for the control, the mock control is 3 to have it be everything that's in the assay 4 but the serum. So control for everything but 5 the one variable. So it then serves as the 6 plaque number to use to compare to the 7 serum-containing samples. 8 Q. So would the -- if you removed 9 the IgG, would that have an effect on the mock 10 control? 11 A. We did do studies where we 12 evaluated the impact of anti-IgG on virus 13 infectivity and did not see that effect in the 14 absence of serum as well as the similar 15 observation from the publication from the FDA 16 on their anti-IgG assay development. So in a 17 practical way, I would not expect an effect of 18 not having the anti-IgG present but for the 19 sake of better control or minimizing variables 20 in the assay, meaning having the only variable 21 be serum dilution, the mock contained 22 everything but the serum. 23 Q. There could have been -- what 24 was done in the original studies in 1972, 25 those are very limited studies. Correct?</p>	<p style="text-align: right;">Page 321</p> <p>1 BY MR. KELLER: 2 Q. So because the IgG would 3 interact with not only mumps antibodies but 4 measles antibodies, rubella antibodies, and 5 antibodies for influenza, RSV, whatever 6 antibodies are in that kid's serum, the rabbit 7 antibodies -- the rabbit anti-IgG is going to 8 interact with that and bind it. Correct? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: It has the 12 potential, the anti-IgG has the 13 potential to bind to any IgG that's in 14 the sera. 15 BY MR. KELLER: 16 Q. So when you did these 17 experiments with or without the IgG and the 18 mock, what indicator virus did you use? 19 A. I don't recall with certainty. 20 Q. Was it Jeryl Lynn 135? 21 A. I have an expectation that that 22 was it, but I don't have a recollection that 23 that was the indicator virus. 24 Q. Do you know whether or not you 25 actually ran 100 pediatric samples for the</p>

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<p style="text-align: right;">Page 322</p> <p>1 validation of the AIGENT? 2 A. I don't recall. 3 Q. Do you recall that those 50 4 samples identified by Antonello, those were 5 samples that were run as part of your 6 developing the assay. Correct? 7 MR. SANGIAMO: Object to the 8 form. Calls for speculation. 9 THE WITNESS: I can't say with 10 certainty that that was once -- I'm 11 sorry, they were once part of the assay 12 development. One arm of the assay 13 development would have included 14 whatever anti-IgG, whatever the 15 conditions were that we wound up using 16 in the assays. The development 17 included different concentrations of 18 anti-IgG, for example, one 19 concentration was chosen for the final 20 assay application. So a subset of the 21 sera would be eligible if the indicator 22 -- if all the other assay conditions 23 and the indicator virus and anti-IgG 24 concentration were the same as what was 25 being used in the eventual assay.</p>	<p style="text-align: right;">Page 323</p> <p>1 BY MR. KELLER: 2 Q. Was it your testimony that these 3 50 samples -- that these 100 samples that are 4 identified here had controls that were used in 5 the actual running of Protocol 007, the same 6 positive controls? 7 MR. SANGIAMO: Object to the 8 form. 9 THE WITNESS: I don't have -- I 10 don't have a recollection of whether 11 they were or weren't. 12 BY MR. KELLER: 13 Q. And if they weren't running the 14 validation samples, would that be a concern 15 for you, if they had controls that were not 16 the same as the controls that were run in the 17 actual SOP, running kids serum in Protocol 18 007? 19 A. I need to defer to Joe Antonello 20 whether those data would be usable for that -- 21 appropriate to include in that. 22 Q. Do you recall -- sorry. Go 23 ahead and finish. 24 A. Whether they would be 25 appropriate to include that combination of</p>
<p style="text-align: right;">Page 323</p> <p>1 Whether those particular samples were 2 included as part of that 50, I can't 3 say for sure. 4 BY MR. KELLER: 5 Q. Except you may have had a 6 different control because the controls were 7 not set until after October of 2000, correct, 8 by CBER? 9 A. I'm sorry, what controls are you 10 referring to. 11 Q. Positive controls? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: The -- my best 15 recollection is that the controls were 16 run in -- so in those development 17 studies, I can't verify, I don't recall 18 if the controls were included in those. 19 The limits to the control sera were 20 set, as best I understand, from the 21 results of the validation study. CBER 22 asked for limits to be set but the date 23 or the limits were set to -- the best 24 that I can recall, was a value that 25 came out of the validation study.</p>	<p style="text-align: right;">Page 325</p> <p>1 data. 2 Q. Do you recall ever hearing that 3 the data that was generated as part of the 4 validation was insufficient to generate 5 reliable data to validate Protocol 007 AIGENT? 6 A. Not that I recall. 7 Q. Would that surprise you to learn 8 that? 9 MR. SANGIAMO: Objection. Form. 10 THE WITNESS: I don't recall 11 hearing that. 12 BY MR. KELLER: 13 Q. Let me direct your attention 14 back to Exhibit 33. On the second page at 15 759837 Dr. Schofield, on October 12, 16 responded to your October 10 e-mail in the 17 middle of the second page. He says, "Some 18 comments highlighted below." If you look on 19 your e-mail at the bottom of 759838, there's a 20 statement that says should the validation also 21 include a requirement for up-front testing to 22 evaluate pre- and post-rates? 23 A. Where are you? 24 Q. Sorry. Right there. 25 A. Okay.</p>

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<p style="text-align: right;">Page 326</p> <p>1 Q. So you wrote, Should the 2 validation also include a requirement for 3 up-front testing to evaluate pre-positive 4 rates (around 10 percent target?) and..., 5 typo, ...seroconversion rates (greater or 6 equal to 95 percent) for a panel of 50 to 7 60...pediatric sera. 8 Do you see that? 9 MR. SANGIAMO: You left out 10 paired. 11 BY MR. KELLER: 12 Q. Pediatric sera. 13 MR. SANGIAMO: You left out 14 paired. 15 BY MR. KELLER: 16 Q. I'm sorry, paired pediatric 17 sera. Thank you. 18 Do you recall writing that? 19 A. It's in an e-mail from me, but I 20 don't have an independent recollection. 21 Q. Below that -- 22 MR. SANGIAMO: Jeff, you did it 23 again. You got to let him finish. 24 THE WITNESS: In the -- I don't 25 have an independent recollection of</p>	<p style="text-align: right;">Page 328</p> <p>1 of the AIGENT? 2 MR. SANGIAMO: Object to the 3 form. 4 THE WITNESS: A goal in the 5 development of the AIGENT was to have 6 an assay that was capable of measuring 7 95 percent seroconversion and had a 8 minimum -- in my mind a minimize or 9 minimal pre-positivity rate, whatever 10 that wound up being. 11 BY MR. KELLER: 12 Q. And the goal was 10 percent -- 13 around 10 percent pre-positive rate. Correct? 14 A. That was at least the target 15 that was in some of the documents. 16 Q. So that's what you -- that's 17 what drove your developing the assay to get to 18 that target. Correct? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: The goal was to 22 find an assay that was capable of 23 meeting those two targets. 24 BY MR. KELLER: 25 Q. Fair enough. Have you ever</p>
<p style="text-align: right;">Page 327</p> <p>1 writing -- the wording is -- looks and 2 says -- it was wording I would use, but 3 I don't have an independent 4 recollection of writing that. 5 BY MR. KELLER: 6 Q. Below that it says, "This would 7 be the 'clinical validation' that I mentioned 8 before. Yes, I think it's useful to reliably 9 establish these characteristics, since these 10 were the metrics that drove your development." 11 Do you see that? 12 A. Yes. 13 Q. So here do you believe that to 14 be Dr. Schofield's comment to your statement 15 about the target of less than 10 percent 16 pre-positives and greater than or equal to 95 17 percent seroconversion? 18 A. It's looks like a different 19 font, see comments highlighted below. So I 20 can't say with 100 percent certainty that 21 that's his comment, but it looks like the 22 comment that was added by someone. 23 Q. So that target, is that 24 consistent with your understanding, your 25 belief that that target drove your development</p>	<p style="text-align: right;">Page 329</p> <p>1 developed an assay where you developed the 2 assay to get a certain result -- 3 MR. SANGIAMO: Object to the 4 form. 5 BY MR. KELLER: 6 Q. -- a predetermined result -- 7 MR. SANGIAMO: Object to the 8 form. 9 BY MR. KELLER: 10 Q. -- before Protocol 007? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: I would not 14 characterize it as getting a 15 predetermined result. I would 16 characterize it as developing an assay 17 to achieve sensitivity that was meeting 18 the requirements for the assay. 19 BY MR. KELLER: 20 Q. Have you done that at Merck in 21 the past where you set a target result for an 22 assay and developed an assay to reach that 23 target? 24 MR. SANGIAMO: Object to the 25 form.</p>

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1 THE WITNESS: Not that I recall,
 2 but I remind you that the target that
 3 was set here was a CBER-imposed target.
 4 MR. KELLER: Let me mark this
 5 next exhibit as Exhibit 34, which is a
 6 document that bears Bates stamp number
 7 1218 through 1221, which is a memo from
 8 Manal Morsy to a series of individuals,
 9 including you, Dr. Krah, regarding a
 10 teleconference with CBER on November 29.
 11 - - -
 12 (Exhibit Krah-34, 11/29/00 Memo,
 13 1218 - 1221, was marked for
 14 identification.)
 15 - - -
 16 BY MR. KELLER:
 17 Q. Do you see that?
 18 A. Yes.
 19 Q. Do you recall -- why don't you
 20 take a minute to review this memo and let me
 21 know when you're done.
 22 MR. KELLER: Off the record so I
 23 can use the restroom real quick.
 24 MR. SANGIAMO: We're going to
 25 take a break, take a break. That's

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1 fine.
 2 VIDEOGRAPHER: The time is now
 3 4:41. This concludes disc five.
 4 - - -
 5 (A recess was taken.)
 6 - - -
 7 VIDEOGRAPHER: The time is now
 8 4:57. This begins disc six. You may
 9 proceed.
 10 MR. KELLER: I'd like to mark
 11 for the record Exhibit 35.
 12 - - -
 13 (Exhibit Krah-35, Plaque
 14 Reduction Neutralization Assay for
 15 Mumps Analytical Validation Protocol
 16 (v.01), 780112 - 780116, was marked for
 17 identification.)
 18 - - -
 19 MR. KELLER: For the record,
 20 Exhibit 35 is a document bearing Bates
 21 stamp number 780112 through 116,
 22 entitled: "Plaque Reduction
 23 Neutralization Assay for Mumps
 24 Analytical Validation Protocol (v.01)."
 25 BY MR. KELLER:

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1 Q. Do you see that?
 2 A. Yes.
 3 Q. Was that your handwriting on
 4 page 2 at 780114?
 5 A. It doesn't look like my
 6 handwriting.
 7 Q. Do you recall on 78 -- back up.
 8 Do you recall ever seeing this
 9 document before, Exhibit 35?
 10 A. I recall there are parts of the
 11 protocol that look familiar to me. Whether I
 12 saw it in its entirety I can't say. In fact,
 13 looking on page 3, looks like it's a draft
 14 version since it has underlining. So I don't
 15 know, depending on who made the edits, if I
 16 would have seen those parts.
 17 Q. So this is a -- this Exhibit 35
 18 is a draft. Correct?
 19 A. I can't say with certainty other
 20 than page 3 and -- on page 3 at least there
 21 are edits made, which would imply a draft.
 22 Q. And so this reference on page
 23 780114 where there's a circle around the 100
 24 pre- and post-vaccination paired pediatric
 25 samples, it says 100 or fewer due to

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1 contamination. Do you believe that half of
 2 the samples that were being proposed to be
 3 tested as part of the pediatric samples were
 4 not usable because of contamination in your
 5 lab?
 6 A. I don't recall.
 7 Q. Let me direct your attention --
 8 A. If I may add to that, at the end
 9 you put in in my lab. The source of the -- if
 10 there was contamination, I do recall some sera
 11 we tested at some point, where there was
 12 contamination was the sera, not something
 13 introduced in the lab.
 14 Q. So it's your testimony that you
 15 recall there being contaminated serum but that
 16 was contaminated from someplace else but not
 17 in your lab. Correct?
 18 A. Yes. I don't recall if it was
 19 this particular set, but I do recall a period
 20 where a panel showed, that we were evaluating,
 21 had a contamination problem.
 22 Q. Let me direct you to the 2001
 23 journals. Can you pull those in front of you?
 24 A. Okay.
 25 Q. If you could direct your

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<p style="text-align: right;">Page 334</p> <p>1 attention to January 21, 2001, at 490623. 2 A. I'm sorry? 3 Q. 490623. January 21, 2001. Do 4 you see that reference to the last entry? Can 5 you read the last entry for me? 6 A. Sorry, on Sunday 21st was that? 7 Q. Yes. Sorry. 8 A. Review Manal's info for CBER. 9 Revise validation protocol to be approximately 10 50 pediatric sera instead of 100. 11 Q. Does that refresh your 12 recollection that you, in fact, were at least 13 editing the validation protocol at this point? 14 A. That indicates that the 15 validation protocol was edited, revised, if 16 you will, on the 21st of January, 2001. 17 Q. And this revision of the 18 protocol from around 50 pediatric sera instead 19 of 100, do you recall that was due to 20 contamination of the sera that you received? 21 A. I don't -- 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: I don't recall the 25 rationale for that change.</p>	<p style="text-align: right;">Page 336</p> <p>1 set number 24 are contaminated - any ideas of 2 the source? 3 Q. So does that lead you to believe 4 that the sera that you had anticipated testing 5 for the validation protocol that we had seen 6 documents earlier where Antonello was 7 recommending running 100 paired samples, and 8 here on January 21st, you reference needed to 9 revise it from 50 -- down from 100 to 50, and 10 in conjunction with the draft protocol in 11 Exhibit 35 where there's a reference to 12 contamination, that, in fact, those 50 samples 13 of sera that you had anticipated to be run for 14 the validation pediatric sera was contaminated 15 and, therefore, you didn't have it and you 16 need to revise the validation protocol for 17 that purpose? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: I can't tell from 21 the wording here. But I can't confirm 22 that that sera set number 24 was 23 intended for the validation study or 24 not. 25 BY MR. KELLER:</p>
<p style="text-align: right;">Page 335</p> <p>1 BY MR. KELLER: 2 Q. Let me direct your attention 3 back to your journal from 2000. If you can go 4 to 490489, which is dated November 14, and ask 5 you questions on the end of that journal entry 6 on 489, which is pages 408 and 409 of your 7 journal, if that helps. 8 A. Yes, okay. 9 Q. So on 409, which is 490489 in 10 the Bates numbers, it says, Assign MMRV-715-00 11 to the receipt of serum set number 24 from 12 Serologic group (from October 31, Kelly 13 Buckley: 60 paired sera...). 14 Do you see that? 15 A. Yes. 16 Q. Did you get the sera for the 17 validation samples from Kelly Buckley? 18 A. I don't recall who we received 19 them from. 20 Q. If you look on 490500, which is 21 page 420 of your -- which is November 25, 22 2000, there's a reference to Saturday. Can 23 you read your Saturday entry? 24 A. Okay. It says, Leave message 25 with Kelly Buckley re most of the sera from</p>	<p style="text-align: right;">Page 337</p> <p>1 Q. But it's fair to say that on 2 January 21st, you have a reference in your 3 journal to revise the protocol to be around 50 4 ped sera instead of 100. Correct? 5 A. I'm sorry, what's the date again 6 for that one? 7 Q. Right here. 8 A. January 21, 2001? 9 Q. Yes. 10 A. Yes. 11 Q. And when you say ped, you mean 12 pediatric? 13 A. Pediatric, yes. 14 Q. So did you revise the validation 15 protocol from 100 to 50? 16 A. I don't recall. 17 Q. Do you recall any discussion 18 with any e-mails from Dr. Schofield stating 19 that if you reduced the number of pediatric 20 serum that were tested in the validation 21 protocol, that the results would be of limited 22 data and unusable? 23 MR. SANGIAMO: Objection. Form. 24 THE WITNESS: I don't recall a 25 discussion on those lines.</p>

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<p style="text-align: right;">Page 338</p> <p>1 MR. KELLER: Let me mark this 2 next exhibit as Exhibit 36. 3 - - - 4 (Exhibit Krah-36, Series of 5 e-mails, 52848 & 5284, was marked for 6 identification.) 7 - - - 8 BY MR. KELLER: 9 Q. Let me back up for a second. 10 You made a point of saying that 11 there was no contamination of sera in your 12 lab. During the time that you were running 13 Protocol 007, you had a very serious problem 14 of mold problems in your incubators, didn't 15 you? Do you remember that? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: I don't -- I 19 remember we had mold occasionally in 20 the incubator, but I don't recall it 21 being at that particular time. 22 BY MR. KELLER: 23 Q. Do you recall having problems 24 in -- at the end of 2000? 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 340</p> <p>1 A. Okay. 2 Q. On the second page of this 3 e-mail there's an e-mail from you, Dr. Krah, 4 dated January 21, 2001, to Emini, Shaw, 5 Washabaugh, Schofield, Heyse, Antonello and 6 Yagodich, Karen Hencken and Jerry Sadoff. Do 7 you see that? 8 A. Yes. 9 Q. And the subject was the 10 "Anti-IgG Enhanced mumps neutralization assay 11 validation protocol draft." 12 Do you see that? 13 A. Yes. 14 Q. Who was Karen Hencken? 15 A. I don't recall. I know of 16 Karen. She's had different positions over the 17 time I knew her. I don't recall her position 18 at the time of this e-mail. 19 Q. Was she involved in -- do you 20 know if she's involved in GMP compliance? 21 MR. SANGIAMO: Object to the 22 form. 23 MR. KELLER: Strike that. 24 BY MR. KELLER: 25 Q. Do you recall if she is involved</p>
<p style="text-align: right;">Page 339</p> <p>1 form. 2 THE WITNESS: I don't recall. 3 BY MR. KELLER: 4 Q. Do you recall having problems 5 in -- during the time that you were running 6 the preliminary subset, having mold problems 7 in your incubators that those samples were run 8 on? 9 A. Not that I recall. 10 Q. But you recall a mold problem in 11 the incubators, just not during that time 12 frame? 13 A. I recall occasional mold in some 14 incubators. Whether they were incubators 15 associated with this testing, I don't recall. 16 And if it was at that time, I don't recall. 17 MR. KELLER: Fair enough. 18 Let me mark this next exhibit. 19 MS. SCANLAN: Marked it already. 20 BY MR. KELLER: 21 Q. Let me mark -- show you 22 Exhibit 36, which is a series of e-mails 23 bearing Bates stamp number 52848 through 24 52849, and feel free to read these e-mails. 25 Let me know when you're done.</p>	<p style="text-align: right;">Page 341</p> <p>1 in any kind of quality control, quality 2 assurance functions? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: At some point 6 of -- the time that I knew her, she 7 wasn't involved in a quality control 8 function. I don't recall at this 9 specific time what her role was. 10 BY MR. KELLER: 11 Q. And here in this e-mail on 12 January 24th you write, "Attached is a draft 13 of the validation protocol, prepared in 14 collaboration with Joe Antonello, for the 15 anti-IgG enhanced mumps plaque-reduction 16 neutralization assay." 17 Do you see that? 18 A. Yes. 19 Q. It says, "This is a slight 20 revision to the one circulated by Manal last 21 week. Please review and return to me with 22 your comments and/or signatures." 23 Do you see that? 24 A. Yes. 25 Q. This one has version .01. And</p>

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<p style="text-align: right;">Page 342</p> <p>1 what I showed you in Exhibit 35 is also 2 version 1. Do you see that? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: Yes. 6 BY MR. KELLER: 7 Q. And so do you recall circulating 8 versions of the draft validation protocol? 9 A. I don't recall. 10 Q. On February 12, about, what is 11 that, three weeks later, you followed up with 12 an e-mail to the same folks, same topic 13 saying, "Please review the attached draft that 14 was sent out in late January and either 15 provide comments or the signed cover 16 (signature) page." It says, I only received 1 17 signature back (and 1 comment from the same 18 person) so far. 19 Do you see that? 20 A. Yes. 21 Q. So on February 15th, based on 22 your prompting, Timothy Schofield responded. 23 Do you see that? 24 MR. SANGIAMO: Object to the 25 form.</p>	<p style="text-align: right;">Page 344</p> <p>1 A. Might have. 2 MR. SANGIAMO: Did you get that, 3 Linda? The document says you might 4 have, not must have. 5 MR. KELLER: I'll reread it. 6 Strike the prior question. 7 BY MR. KELLER: 8 Q. Comment: On page 3 (and in the 9 last section) you mention using the data that 10 you collect on the controls to establish 11 controls limit. This will be far too little 12 data to set reliable limits. You might add 13 that "The control criteria will be updated 14 after a sufficient number of runs have been 15 performed, to obtain reliable estimates of 16 assay performance (total N equal 20 runs)." 17 Do you see that? 18 A. Yes. 19 Q. Did you address that language to 20 the draft protocol? 21 A. I don't recall. 22 Q. And so if you go back to 23 Exhibit 35, can you tell what he's talking 24 about? Page 3, in the last section. Is he 25 talking about the seroclassification cutoff?</p>
<p style="text-align: right;">Page 343</p> <p>1 THE WITNESS: I see a reply from 2 him, yes. And he says -- 3 MR. SANGIAMO: Wait, hold on a 4 second. Did you finish your answer, 5 Doctor? 6 THE WITNESS: I see a reply 7 following as listed on the 8 February 15th. 9 BY MR. KELLER: 10 Q. And here it says, Schofield 11 states, "David, I reviewed the protocol, and 12 have one comment, and a couple of typos. 13 Comment: On page 3 (and in the 14 last section) you mention using the data that 15 you collect on the controls to establish 16 control limit. This will be far too little 17 data to set reliable units. You must add that 18 "The control criteria will be updated after a 19 sufficient number of runs have been performed, 20 to obtain reliable estimates of assay 21 performance (total N equals 20 runs)." 22 Do you see that? 23 A. You used the word must, you must 24 add. I'm sorry. 25 Q. You might have.</p>	<p style="text-align: right;">Page 345</p> <p>1 A. My understanding and recollection 2 of what he was referring to there are the 3 control limits, second paragraph, Each 4 validation run will also include testing on 5 the mock control, and in parentheses, and on 6 low and high positive control samples (adult 7 sera)..., as I recall discussion with Joe 8 Antonello when the validation report was being 9 assembled that -- my understanding, my 10 recollection of the procedure that he would 11 follow would be a tentative control limit 12 would be set based on the available data that 13 number or value, or values, if there are 14 multiple controls, would be updated as more 15 data became available. 16 Q. And the data, as more data 17 became available, is that running sera from 18 Protocol 007 or running sera from sera outside 19 of Protocol 007? 20 A. My understanding of that comment 21 and best recollection is that that refers to 22 the adult -- the positive control sera which 23 are adult lab volunteer sera. So sera outside 24 of Protocol 007. 25 Q. So your testimony is that these</p>

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<p style="text-align: right;">Page 346</p> <p>1 20 runs were supposed to be sera outside of 2 Protocol 007 sera. Correct? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: I don't believe 6 you're capturing the assay format 7 accurately. In a given assay, sera 8 from a given study can be tested and 9 there are control sera tested. So 10 these are not 20 assays of only control 11 sera but 20 assays, as best I 12 understand this, 20 assays in which 13 control sera were included. 14 BY MR. KELLER: 15 Q. That control sera, you said that 16 would include the mock? 17 A. Sorry, that -- in the paragraph 18 it's listed as one of the controls, but the 19 control sera that, my understanding, Tim 20 Schofield is referring to are the positive 21 control sera. 22 Q. The adult sera? 23 A. The adult sera, the lab 24 volunteers. 25 Q. You don't think he was talking</p>	<p style="text-align: right;">Page 348</p> <p>1 mumps for the AIGENT? 2 MR. SANGIAMO: Object to the 3 form. 4 THE WITNESS: It's version .02 5 of at least -- from the title version 6 .02 of the "Plaque Reduction 7 Neutralization Assay for Mumps 8 Analytical Validation Protocol." 9 BY MR. KELLER: 10 Q. Is this the final? 11 A. It's marked -- sorry. The 12 signatures are initial review. I cannot tell 13 from the document whether it's final or not. 14 Q. If you look on the first page, 15 that's your signature. Correct? 16 A. Yes. 17 Q. That's February 12, 2001, when 18 you signed this? 19 A. 21st of -- February 21, 2001. 20 Q. And what was the date of the 21 last signature? Is that March 6, 2001? 22 A. Looks like -- March 6th looks 23 like the last signature. 24 Q. In the first paragraph of the 25 signature part of this validation protocol, do</p>
<p style="text-align: right;">Page 347</p> <p>1 about the reduction from 100 pediatric sera 2 down to 50? 3 A. My reading of this and my 4 recollection of this was that he was referring 5 to the number of runs that we had with the 6 control sera. So it was not related to the 7 dropping from 100 to 50 but was referring to 8 how many assays in which the adult lab 9 volunteer control sera were run. 10 MR. KELLER: Let me mark the 11 next exhibit as Exhibit 37. 12 - - - 13 (Exhibit Krah-37, Plaque 14 Reduction Neutralization Assay for 15 Mumps Analytical Validation Protocol 16 (v.02), 337307 - 337318, was marked for 17 identification.) 18 - - - 19 MR. KELLER: For the record, 20 Exhibit 37 is a document that bears 21 Bates stamp number 337307 through 318. 22 BY MR. KELLER: 23 Q. Can you tell me if you recognize 24 this document as the -- as a version of the 25 plaque reduction neutralization assay for</p>	<p style="text-align: right;">Page 349</p> <p>1 you recall whether or not there was a final 2 validation protocol different from this 3 exhibit? 4 MR. SANGIAMO: Object to the 5 form. 6 THE WITNESS: I don't recall. 7 BY MR. KELLER: 8 Q. Here it says, quote, the final 9 review is not circled, only the initial 10 review. Do you see that on the first page? 11 A. Yes. 12 Q. You don't recall ever seeing a 13 final review that was circled. Correct? 14 A. I don't recall. 15 Q. Here it says in the first 16 paragraph, Your signature below indicates your 17 acceptance of a validated protocol -- of the 18 attached validation protocol, given that no 19 comments are provided by any of the reviewers. 20 If comments are received, the protocol will be 21 revised and recirculated, with the comments 22 appropriately incorporated or addressed. Do 23 you see that? 24 A. Yes. 25 Q. Can you turn your attention to</p>

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<p style="text-align: right;">Page 350</p> <p>1 page 337314, Karen Hencken. 2 A. Okay. 3 Q. So she is identified as a "World 4 Wide Quality Assurance." Do you see that? 5 A. Yes. 6 Q. She checked off "Comments." Do 7 you see that? 8 A. There is a check mark next to 9 comments. 10 Q. Here under your instructions for 11 signing this document it states that if 12 comments are received, the protocol will be 13 revised and recirculated, with the comments 14 appropriately incorporated or addressed. Do 15 you see that on the first page, on every 16 signature page? 17 A. Yes. 18 Q. Would you be -- would you expect 19 that since Karen Hencken had checked the box 20 as having comments, that there would have been 21 another version of this based on the 22 instructions of this signature page? 23 A. I would not say -- given the 24 wording that is here, I would not say with 25 certainty that a new version would be issued,</p>	<p style="text-align: right;">Page 352</p> <p>1 MR. SANGIAMO: Objection to the 2 form. You said produced. 3 MR. KELLER: Sorry. I'll start 4 over. Getting tired here. Strike my 5 last question. 6 BY MR. KELLER: 7 Q. "It is understood that these 8 experiments will be performed in a GLP 9 compliant laboratory to ensure the validity of 10 the data." 11 Do you see that? 12 A. Yes. 13 Q. Do you know whether or not these 14 submissions were ever given to CBER? 15 A. I don't -- that, I don't know. 16 Q. Who -- do you know, was that 17 something that you put into the signature 18 page, this is only done pursuant to a GLP 19 compliant laboratory and not a GMP or G -- 20 Good Clinical Practices laboratory? 21 MR. SANGIAMO: Object to the 22 form. 23 MR. KELLER: Strike that. 24 BY MR. KELLER: 25 Q. This reference to GLP, do you</p>
<p style="text-align: right;">Page 351</p> <p>1 but indicates that the protocol would be if 2 comments are received, the protocol will be 3 revised and circulated, with comments 4 appropriately incorporated or addressed. If 5 they're addressed in a way that doesn't 6 require incorporation, it may not require a 7 new version. In this case, I can't speak to 8 what the comments were or whether a new 9 version was issued. 10 Q. You don't know -- you don't 11 recall what her comments were? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: At least from this 15 document, I don't see, or nothing 16 looks -- I don't have any indication 17 what the comments were. 18 BY MR. KELLER: 19 Q. If you go on in the signature 20 instructions, in the first -- in front of 21 every signature page it says, It is understood 22 that these experiments will be produced in a 23 GLP compliant laboratory to ensure the 24 validity of the data. Do you see that? 25 A. Yes.</p>	<p style="text-align: right;">Page 353</p> <p>1 recall who put that in the signature line? 2 A. I don't -- 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: -- recall with 6 certainty. I don't recall that I put 7 that in there. 8 BY MR. KELLER: 9 Q. And that really is -- that's a 10 true statement, that your lab was only 11 compliant to GLP. Correct? Strike that. 12 Was your lab compliant with the 13 GLP requirements -- 14 MR. SANGIAMO: Object to the 15 form. 16 BY MR. KELLER: 17 Q. -- as of the date of this 18 document? 19 A. At this moment I'd say -- my 20 understanding of GLP is not extensive, so I 21 can't comment on whether we were or weren't 22 compliant with GLP. 23 Q. Let me direct your attention to 24 the body of the protocol. Have you -- when 25 was the last time you reviewed this protocol?</p>

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1 A. I don't recall.
 2 Q. I assume you read it before you
 3 signed it. Correct?
 4 A. Yes.
 5 Q. If you want to take a minute to
 6 review this protocol, why don't you do that.
 7 Let me know when you're done.
 8 A. Okay.
 9 Q. Let me direct your attention to
 10 page 2 where it says, "Assay Validation
 11 Experiments."
 12 Do you see that?
 13 A. Yes.
 14 Q. Here it says, The plaque
 15 reduction neutralization assay will be
 16 performed according to the Department of Virus
 17 Biologic Research Procedure Number 474.3489,
 18 rev. 00 ("Anti-IgG Enhanced Mumps
 19 Plaque-Reduction Neutralization Assay").
 20 Do you see that?
 21 A. I do. It's 874.3679. You said
 22 4.
 23 Q. Sorry. I apologize. 874- --
 24 .3489. Correct? That's the SOP for the
 25 AIGENT. Correct?

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1 MR. SANGIAMO: You also
 2 misidentified the department. You said
 3 virus and biologic research. It's
 4 virus and cell biologic research.
 5 MR. KELLER: Strike that whole
 6 thing.
 7 BY MR. KELLER:
 8 Q. Dr. Krah, under "Assay
 9 Validation Experiments," the second sentence
 10 it says, "The validation experiment will
 11 include sera from 4 adults and approximately
 12 50 pre- and post-vaccination paired pediatric
 13 samples."
 14 Do you see that?
 15 A. Yes.
 16 Q. And in the prior draft of this
 17 protocol on Exhibit 35, on page 870114, it
 18 said, "...100 pre- and post-vaccination paired
 19 pediatric samples," and circled is a reference
 20 to "or fewer due to contamination."
 21 Do you see that?
 22 A. Yes. In the document 780114.
 23 Q. Do you recall that the number of
 24 pediatric sera that was proposed went from 100
 25 down to 50 because of a problem with the sera

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1 that was going to be used to run those
 2 experiments?
 3 A. I can't -- I don't recall with
 4 certainty.
 5 Q. Would you -- would it be fair to
 6 say that the protocol reduced by half the
 7 number of pediatric sera to be tested as part
 8 of the validation experiments from what was
 9 proposed by Joe Antonello in October of 2000
 10 to what ended up in the final or in this draft
 11 of the validation protocol?
 12 A. I would say numerically I can't
 13 see if there are other pediatric sera included
 14 in this, but it looks, at least from my
 15 reading of it, approximately half the number
 16 of pre- and post-vaccination paired pediatric
 17 samples were included, but I would point out
 18 that amongst the evaluation or the validation
 19 evaluations, the -- I'm sorry, the validation
 20 evaluations, it looks like the pediatric
 21 samples will be divided among multiple assay
 22 runs that is not a number reduced from the
 23 original proposal.
 24 Q. So is it your testimony, sir,
 25 that there was 100 paired samples tested of

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1 pediatric serum as part of this validation
 2 protocol?
 3 MR. SANGIAMO: Objection.
 4 Misstates testimony.
 5 THE WITNESS: No, that's not
 6 what I was saying.
 7 BY MR. KELLER:
 8 Q. So these runs that you're
 9 saying, the 50 runs that you're talking about,
 10 are you testifying that those 50 runs
 11 represent 100 pairs of pediatric samples?
 12 MR. SANGIAMO: Objection.
 13 Misstates the testimony.
 14 THE WITNESS: What I'm
 15 representing is that there are -- this
 16 is written that there are
 17 approximately, in addition to the four
 18 adults here, there's approximately 50
 19 pre- and post-vaccination paired sera.
 20 Pediatric samples will be divided among
 21 the next -- sorry, the first paragraph
 22 on page 337317, "The pediatrics samples
 23 will be divided among multiple (7)
 24 assay runs with pre- and
 25 post-vaccination sample pairs being

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<p style="text-align: right;">Page 358</p> <p>1 tested together in the same assay run." 2 That the number of replicate runs is 3 not reduced from the original proposal. 4 BY MR. KELLER: 5 Q. So it's your understanding that 6 there would be additional samples run as part 7 of this validation protocol in order to -- is 8 it -- strike that. 9 Is it your belief that because 10 it says, "The pediatric samples will be 11 divided among multiple (7) assay runs...," 12 that that was going to happen in the future? 13 A. My understanding and my 14 interpretation of that is that those -- the 50 15 pre- and post-vaccination serum pairs would be 16 split up among seven different assays. 17 Q. Did you believe as of the date 18 of this -- 19 MR. SANGIAMO: I'm sorry, Jeff. 20 BY MR. KELLER: 21 Q. I didn't mean to cut you off. 22 A. As part of this -- as part of 23 the validation. 24 Q. I see. Did you understand that 25 those runs were already -- those assay runs</p>	<p style="text-align: right;">Page 360</p> <p>1 specification limits for the mock and positive 2 control samples. 3 Do you see that? 4 A. Yes. 5 MR. SANGIAMO: Object to the 6 form. 7 BY MR. KELLER: 8 Q. Did you understand that the mock 9 control samples that they're talking about 10 there, that they were all run in pediatric 11 samples, in those 50 paired samples run over 12 seven assay runs? 13 A. I'm sorry, the mock is an 14 inherent part of each assay, so it would be 15 run in every assay regardless of what sera are 16 tested. 17 Q. I see. So the control criteria 18 will be updated after a sufficient number of 19 runs have been performed to obtain reliable 20 estimates of assay performance (N equals 20 21 runs). 22 Do you see that? 23 A. Yes. 24 Q. That's what Schofield had 25 recommended that you put into the protocol.</p>
<p style="text-align: right;">Page 359</p> <p>1 were already completed by the time you drafted 2 this protocol? Correct? Strike that. 3 Those experiments, those 50 4 paired serum through seven assay runs were 5 already completed when this protocol, 6 validation protocol was signed. Correct? 7 A. I can't say that with certainty. 8 Q. Well, Joe Antonello on 9 October 30th said we've already run half of 10 them. Right? So half of the 50 -- half of 11 the 100 is 50. Correct? 12 A. I can't say with certainty that 13 the 50 that he's referring to is the 50 that 14 we wound up using. 15 Q. I see. And so he goes on in the 16 next paragraph to state that, Each validation 17 run will include testing on the mock control, 18 and on the positive control sample (adult 19 sera). Note that some of the pediatric serum 20 assays and specificity assays include a single 21 control serum. All assays of clinical sera 22 will include two control sera (low and high 23 titer). The data arising from the validation 24 experiment will be used to establish assay 25 validity criteria in the form of tentative</p>	<p style="text-align: right;">Page 361</p> <p>1 Correct? 2 A. That looks like -- appears to be 3 the wording that he recommended, at least N 4 equals 20 runs, and updating it -- updated 5 after a sufficient number of runs had been 6 performed. 7 Q. You don't know whether or not 8 those runs were from runs using Protocol 007 9 sera or runs using sera from -- that Merck had 10 acquired through other sources? 11 MR. SANGIAMO: Object to the 12 form. 13 THE WITNESS: I don't recall 14 which sera were -- 15 BY MR. KELLER: 16 Q. Can you -- as you sit -- 17 MR. SANGIAMO: Jeff. 18 BY MR. KELLER: 19 Q. I'm sorry. Go ahead. 20 A. I don't recall which sera 21 were -- where the source -- I can't tell from 22 this document what the source of the pediatric 23 sera was. 24 Q. As you sit here today, do you 25 see any problems with Merck using the sera</p>

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<p style="text-align: right;">Page 362</p> <p>1 from Protocol 007 to run those 20 runs? 2 MR. SANGIAMO: Object to the 3 form. 4 THE WITNESS: I have a general 5 understanding of the -- sorry, I'm not 6 familiar with the specific requirements 7 for a validation study. I have 8 a general perception, this is personal 9 perception, that the sera from a 10 pediatric sera -- the pediatric sera 11 from a clinical study would not be used 12 as part of a validation study. That 13 would not apply, in my view, to adult 14 lab volunteer sera. 15 BY MR. KELLER: 16 Q. Correct. Because those adult 17 sera are not run in the Protocol 007 sera. 18 Those are Protocol 007 sera from the kids that 19 were gathered as part of the protocol in the 20 study. Correct? 21 MR. SANGIAMO: Object to the 22 form. 23 BY MR. KELLER: 24 Q. Strike that. That was a 25 terrible question. I'll leave it at that.</p>	<p style="text-align: right;">Page 364</p> <p>1 you, Dr. Krah, dated December 10, 2001. 2 Actually two of your e-mails. I'll draw your 3 attention to the first e-mail on December 10th 4 at 12:22 p.m. 5 A. I'm sorry, what was that? 6 Q. The third paragraph down. 7 A. Bottom e-mail, okay. 8 MR. SANGIAMO: Read the e-mail. 9 BY MR. KELLER: 10 Q. You write, "The testing of 11 the..." -- 12 MR. SANGIAMO: Hold on, he 13 hasn't read it. 14 MR. KELLER: I'll read it. 15 MR. SANGIAMO: He hasn't read 16 the e-mail. 17 MR. KELLER: He can read it. 18 MR. SANGIAMO: He's going to 19 read a particular paragraph and when 20 he's done reading the e-mail, then you 21 ask the question. 22 BY MR. KELLER: 23 Q. I'm just going to ask you 24 questions about this one sentence. It says, 25 quote, The testing of the interim analysis set</p>
<p style="text-align: right;">Page 363</p> <p>1 Let me have you turn -- did you 2 ever discuss with Joe Antonello those -- I 3 showed you a document earlier where you state 4 you started running samples in Protocol 007 on 5 December 6, 2000. Do you recall that? 6 A. I don't recall the specific 7 date. 8 Q. Do you recall that you were 9 already running clinical samples from Protocol 10 007 during the time that you were validating 11 the protocol? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: I'm not able to 15 confirm dates. 16 MR. KELLER: Let me mark the 17 next exhibit, Exhibit 38, which bears 18 Bates stamp number 52242. 19 - - - 20 (Exhibit Krah-38, 12/10/99 21 E-mails, 52242, was marked for 22 identification.) 23 - - - 24 BY MR. KELLER: 25 Q. It's a single-page e-mail from</p>	<p style="text-align: right;">Page 365</p> <p>1 started on December 6, 2000, and ended 2 January 26, 2001. 3 My question is, is that a true 4 and correct statement as to when the sera from 5 Protocol 007 preliminary subset was run? 6 That's all I want to ask about this document. 7 MR. SANGIAMO: Read the e-mail 8 and then answer the question. 9 MR. KELLER: He doesn't need to 10 read the entire e-mail to do that, but 11 go ahead. 12 THE WITNESS: I can't verify 13 this independently, but I interpret 14 that next to -- the next to the last 15 paragraph to mean that no testing of 16 protocol sera was started prior to the 17 start date listed as 06, December 2000. 18 BY MR. KELLER: 19 Q. That's not my question. My 20 question is -- okay. That's fine. 21 MR. SANGIAMO: That is your 22 question. 23 MR. KELLER: That is my 24 question. You're right. Got you. 25 BY MR. KELLER:</p>

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1 Q. So is it -- other than this
 2 e-mail, you don't recall starting -- running
 3 samples from Protocol 007 before you had
 4 validated the SOP. Correct?
 5 MR. SANGIAMO: Object to the
 6 form.
 7 THE WITNESS: I don't recall the
 8 dates. This has listed dates for the
 9 validation. There are assays to
 10 evaluate variability inter and
 11 intraassay for the adult lab sera panel
 12 that are after that start date.
 13 BY MR. KELLER:
 14 Q. And so going back to Exhibit 38,
 15 the assays that are identified here, it
 16 says -- you write to Alan Shaw, "The following
 17 summarizes the timing of the experiments done
 18 to support validation studies of the mumps
 19 AIGENT assay."
 20 Do you see that?
 21 A. Yes.
 22 Q. Those are the validation studies
 23 that are -- that were to be run -- described
 24 in the validation protocol?
 25 MR. SANGIAMO: Object to the

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1 form.
 2 THE WITNESS: I can say that --
 3 would say that those are experiments
 4 that are -- experiments done in support
 5 of the validation studies that would be
 6 part of the validation protocol.
 7 Whether this is all inclusive, I can't
 8 say.
 9 BY MR. KELLER:
 10 Q. Do you have any reason to
 11 believe that this is not the list of
 12 experiments that were used to validate
 13 Protocol 007's AIGENT?
 14 MR. SANGIAMO: Object to the
 15 form.
 16 THE WITNESS: All I can tell
 17 you, this lists assays that are
 18 indicated in support of validation
 19 studies. I don't have any information
 20 to the contrary that they were not part
 21 of what was used in the validation
 22 protocol.
 23 BY MR. KELLER:
 24 Q. Let me bring you back to your
 25 journal of February 15, 2001, after you signed

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1 the validation protocol. February 15, 2001,
 2 was before the final signature on the
 3 validation protocol of March 6, 2001.
 4 Correct?
 5 A. I believe the --
 6 Q. This is before you even signed
 7 the validation protocol. Correct?
 8 A. Let's see. I signed it
 9 February 21st of 2001.
 10 Q. Can I direct your attention to
 11 February 15th in your journal which is at
 12 490641 -- 640. Let me know when you're there.
 13 A. 641?
 14 Q. Right. 640, Tuesday,
 15 February 15th, do you see that? Or Thursday,
 16 February --
 17 A. Thursday.
 18 Q. I mean Thursday, February 15,
 19 2001. The second page of that, there is a
 20 reference to you having a meeting with
 21 Dr. Emini at 1:30 p.m. to update the MPS Nt
 22 data. Do you see that?
 23 A. Yes.
 24 Q. Do you recall -- you testified
 25 earlier that you recall having a meeting with

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1 Dr. Emini regarding him describing a warning
 2 letter. Can you read, for the record, what
 3 you wrote in your journal?
 4 MR. SANGIAMO: Object to the
 5 preamble. If you want him to read
 6 what's written in the journal, that's
 7 fine.
 8 BY MR. KELLER:
 9 Q. Out loud, please.
 10 A. What it says, it's a meeting
 11 with Emilio 1:30 p.m. to update the mumps neut
 12 data. Merck has been issued a "warning
 13 letter" from the FDA regarding mumps titers
 14 data - The data that we have generated will be
 15 needed to include in the response (due within
 16 14 days from receipt) to provide a "comfort
 17 factor" with the vaccine dose. The full data
 18 set from Protocol 007 would be needed to
 19 change the label/license.
 20 Q. Do you recall that conversation
 21 with Mr. -- with Dr. Emini?
 22 A. I have a recollection of a
 23 meeting where Emilio mentioned the warning
 24 letter. I don't recall all the other aspects
 25 that are in this journal entry.

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1 Q. So your reference to comfort
 2 factor in quotes, you don't recall what he
 3 said about that?
 4 A. No, I don't.
 5 Q. Do you recall -- but you
 6 understood that the results of the preliminary
 7 subset would be used to respond to a warning
 8 letter from the FDA. Correct?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: My interpretation
 12 is that, as it says, the data that we
 13 have will be needed. I don't know what
 14 needed means. Needed to include.
 15 BY MR. KELLER:
 16 Q. Do you recall whether or not the
 17 results of the preliminary subset that was run
 18 by your lab was submitted to the FDA in
 19 response to the warning letter?
 20 A. I recall that the data, or at
 21 least my -- I recall that the data from that
 22 subset analysis were provided. Whether it was
 23 in response to the warning letter, I can't say
 24 with certainty.
 25 Q. In the reference here to the

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1 full data set from Protocol 007 being needed
 2 to change the label/license. Do you
 3 understand what you meant when you wrote that?
 4 A. No.
 5 Q. Do you recall what Protocol 007,
 6 the purpose of Protocol 007 was to change the
 7 end expiry specifications for the mumps
 8 component of the MMR II product?
 9 MR. SANGIAMO: Object to the
 10 form.
 11 THE WITNESS: My understanding
 12 of the purpose of the study was to
 13 compare the immunogenicity of three
 14 different doses of mumps. As far as
 15 what it's -- the data would be used
 16 for, I don't have a recollection.
 17 BY MR. KELLER:
 18 Q. Let me direct your attention to
 19 February -- your February 21, 2001, journal
 20 entry on Wednesday, which is 490648.
 21 A. Okay.
 22 Q. If you direct your attention to
 23 page 490650, there's a reference to Robin.
 24 "Robin indicates that she expects to have a
 25 draft validation report Thursday/Friday."

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1 Do you see that?
 2 A. "...draft validation report
 3 Thursday/Friday."
 4 Q. So Robin -- that's Robin
 5 Wolchko. Correct?
 6 A. The sentence -- there are a
 7 couple of sentences before it, it says, "Note:
 8 all data sent to Robin Wolchko...." I don't
 9 know any other Robin.
 10 Q. And Robin -- sorry, I didn't
 11 mean to cut you off.
 12 A. That is the Robin.
 13 Q. Robin worked -- she worked with
 14 Joe Antonello working on the validation
 15 report. Correct?
 16 A. As best I can recall, she was on
 17 the validation report, one of the authors of
 18 the validation report along with Joe
 19 Antonello.
 20 Q. Here, can you read what you
 21 wrote under that statement about her having a
 22 draft validation report Thursday/Friday?
 23 Strike that.
 24 Does this indicate that you had
 25 a conversation with Robin Wolchko --

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1 MR. SANGIAMO: Object to the
 2 form.
 3 BY MR. KELLER:
 4 Q. -- on February 21, 2001? Is
 5 that a fair statement, to say that you spoke
 6 to Robin on that date regarding the draft
 7 validation report?
 8 A. All I can say is that she
 9 indicated she expects to have a draft
 10 validation report Thursday or Friday which
 11 would indicate some communication. Whether it
 12 was a conversation or e-mail, I don't know.
 13 Q. Can you read what you wrote
 14 under that?
 15 A. It says, "I commented on my
 16 observations from the Protocol 007 serum set
 17 assays-mock value 8.67 was not...," there's a
 18 typo of some kind Y-E-D. I don't know what
 19 that -- might be -- I don't know what that is.
 20 Comma, ...and all other runs were
 21 approximately 10.25 to 30.5 pfu for mock;
 22 control sera were with a range of fourfold
 23 across all assays.
 24 Q. Is it fair to say that at this
 25 point on February 21st, you were updating

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<p style="text-align: right;">Page 374</p> <p>1 Robin about your observations from running the 2 serum from Protocol 007? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: I take the comment 6 to mean that I was providing feedback 7 to her on how the mock value was 8 performing in the assays. Not the 9 assays overall, but just what the mock 10 pfu value was. 11 BY MR. KELLER: 12 Q. And the assays you're referring 13 to are the serum that was run as part of 14 Protocol 007. Correct? 15 MR. SANGIAMO: Object to the 16 form. 17 THE WITNESS: No. They're in 18 assays where serum was tested. The 19 mock results are in the absence of 20 serum. 21 BY MR. KELLER: 22 Q. But those are in the Protocol 23 007 experiments, correct, the kids serum in 24 Protocol 007? 25 MR. SANGIAMO: Object to the</p>	<p style="text-align: right;">Page 376</p> <p>1 "Note: signatures were....," can you read the 2 next reference? 3 A. Yes. Note: Signatures were 4 received from first round of reviews of 5 validation protocol from everyone except Jerry 6 Sadoff. 7 Q. In the validation version .02 8 that we have as Exhibit 37, he didn't sign the 9 protocol, the validation protocol, did he? 10 A. I see next to his name an NA. 11 Q. And is that your handwriting, 12 the NA? 13 A. That looks like, yeah, that's my 14 handwriting. 15 Q. And did you talk to Dr. Sadoff 16 as to why he didn't sign the validation 17 protocol? 18 A. I cannot say with certainty, but 19 I can say I would not have put NA next to his 20 name without some feedback on whether that was 21 appropriate. 22 Q. Did Dr. Sadoff voice any 23 reservations about signing the protocol? 24 A. Not that I recall. 25 Q. Did you get his approval to</p>
<p style="text-align: right;">Page 375</p> <p>1 form. 2 THE WITNESS: They're data from 3 experiments in which Protocol 007 were 4 tested but not directly involving -- 5 they're not data from the clinical 6 sera. 7 BY MR. KELLER: 8 Q. I see. But you were updating 9 Robin about your experience from running the 10 Protocol 007 assay using the SOP and the 11 AIGENT. Correct? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: Yes, but only in 15 the context of what the mock value 16 was -- 17 BY MR. KELLER: 18 Q. And in the content of that -- I 19 see what you're saying. Then it goes on to -- 20 MR. SANGIAMO: Did you finish 21 your answer? 22 THE WITNESS: I was going to say 23 the mock values in those assays. 24 BY MR. KELLER: 25 Q. I see. And the next you have a</p>	<p style="text-align: right;">Page 377</p> <p>1 write NA next to that -- his name on the 2 protocol? 3 A. I don't recall. 4 Q. Let me direct your attention to 5 the next day, which is February 22nd, there's 6 a reference in the middle of 490650 to a 7 Meeting at 1:00 for our lab and Emilio... do 8 you see that? "... (in his office)." 9 A. Yes. 10 Q. Do you recall that meeting 11 happening? 12 A. I recall meetings with Emilio. 13 I don't recall what that particular meeting 14 was about. 15 Q. Do you recall a meeting with 16 Emilio where there was discussions of bonuses 17 if the Protocol 007 assay was completed 18 successfully? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: I do not recall 22 that discussion. 23 BY MR. KELLER: 24 Q. Let me direct your attention to 25 the next page at 490651 which is the day after</p>

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<p style="text-align: right;">Page 378</p> <p>1 you spoke to Robin. There's a reference in 2 the middle at top of the page, it says, "Reply 3 to Joe Antonello's phone call..." 4 Do you see that? 5 A. I'm sorry, 1651? 6 Q. Right here. Do you see that? 7 A. Okay. 8 Q. So under that -- can you read 9 what you wrote under that? 10 A. Yes. It says, "Extravariability 11 evaluation - he can add this to our 12 spreadsheets? I proposed - not for current 13 set - no time to reevaluate and reaudit." 14 Q. So this was for the preliminary 15 subset, you were not going to use whatever 16 extravariability flags that were set up on a 17 preliminary subset. Were those run? Is that 18 true? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: I can't tell with 22 certainty what set that applies to. 23 BY MR. KELLER: 24 Q. And under that you say, "For the 25 plaque count limit proposed by CBER." Can you</p>	<p style="text-align: right;">Page 380</p> <p>1 actually proposed the limit or said we 2 would like a limit. So as I -- my 3 first thought was that there may have 4 been a limit that CBER suggested, but 5 in reading this, I'm -- my understanding 6 is that he's suggesting ten is a lower 7 limit, and the upper limit there's some 8 exchange of what we mutually agree 9 would be a suitable upper limit. 10 BY MR. KELLER: 11 Q. Is he proposing ten or are you 12 proposing ten? 13 A. He is proposing ten. 14 Q. How do you get that? Is that 15 something you recall or just how you read 16 this? 17 A. I don't -- it would not be a 18 limit that I would have a basis on providing 19 or generating. I recall subsequent 20 discussions with him to understand his 21 rationale for ten is a lower limit. 22 Q. So you weren't proposing using 23 ten? 24 A. To the best of my recollection, 25 Joe was the one, Joe Antonello was the one</p>
<p style="text-align: right;">Page 379</p> <p>1 read that? 2 A. Yes. It says, "use 10 as lower 3 limit. For upper limit, he proposes using 4 whatever is the upper counting range (50-60?). 5 50 seems okay to me (although a range of 10 to 6 40 seems best to me, as an average of 20 plus 7 or minus twofold range)." 8 Q. So you're -- can you tell me 9 what you're doing here when you're -- this 10 is your -- this is a conversation you're 11 having with Joe Antonello. Correct? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: There is a 15 proposal that -- and I don't recall the 16 specific CBER proposal of a limit that 17 suggests for the plaque count limit 18 based on the validation study that Joe 19 analyzed he is proposing. A limit, and 20 I don't -- I can't tell from this 21 what -- how that -- actually how that 22 compares to CBER's description. But as 23 I'm reading this, the wording is such 24 for the plaque count limit proposed by 25 CBER. I don't recall that CBER</p>	<p style="text-align: right;">Page 381</p> <p>1 proposing ten as the lower limit. 2 Q. You discussed with him the upper 3 limit. He talked about 50 to 60 and you said 4 10 to 40 seems best to you. Correct? 5 MR. SANGIAMO: Object to the 6 form. 7 THE WITNESS: That's what it 8 says there. 9 BY MR. KELLER: 10 Q. Is there any clinical 11 significance to the mock control range? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: Not that I'm aware 15 of. 16 BY MR. KELLER: 17 Q. Is that used to set the 18 serostatus cutoff? 19 A. No. 20 Q. What is the mock range set 21 for -- what is it used for in an assay? 22 A. It is used to calculate the 23 percent value -- percent plaque numbers for 24 test sample relative to a -- to the mocks and 25 then determine whether a sample is</p>

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<p style="text-align: right;">Page 382</p> <p>1 neutralizing or not. 2 Q. So whether or not it's a -- the 3 sample is a seroconverter or 4 non-seroconverter. Correct? 5 MR. SANGIAMO: Object to the 6 form. 7 BY MR. KELLER: 8 Q. It's used in that calculation. 9 Correct? 10 A. Not directly. It's used on an 11 individual sera basis to calculate the number 12 of plaques as a percent of the mock value. So 13 it identifies whether a given serum, it 14 identifies the titer for a given serum. The 15 seroconversion is a second calculation. 16 Q. And does the 10-40 play into 17 that calculation at all? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: The range is only 21 used, from my understanding, to 22 calculate the plaque count toward test 23 sample relative to the mock for a given 24 serum sample. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 384</p> <p>1 780093 & 780094, was marked for 2 identification.) 3 - - - 4 BY MR. KELLER: 5 Q. Let me mark as Exhibit 39 a 6 document that bears Bates stamp numbers 780093 7 through 94. It's a fax from you, Dr. Krah, to 8 Joe Antonello, dated February 22, 2001. And 9 is that your handwriting on the second page? 10 A. Yes, it looks like my handwriting. 11 Q. Is this what you faxed to Joe 12 Antonello that's referenced in your journal on 13 February 22, 2001? 14 A. I don't have an independent 15 recollection of it. It indicates I'm sending 16 a summary of the mock serum pfu and titers for 17 MKY and CM serum, which is included in the 18 data on the back of page 2 of that. So I 19 can't independently confirm it, but it looks 20 consistent with what was on the -- is on the 21 back pages, captures the same classification 22 or categories of data. 23 Q. So looking at -- this is your 24 handwriting, though. Correct? 25 A. Yes.</p>
<p style="text-align: right;">Page 383</p> <p>1 Q. So later on you write, "Fax 2 summary of results from Protocol 007 testing 3 to Joe Antonello...mock pfu, MKY titer, CM 4 titer, by assay." 5 Do you see that? 6 A. Yes. 7 Q. Why did you submit that data to 8 Joe Antonello? 9 A. I can't say with certainty. I 10 have an expectation of that, but I don't -- I 11 can't say with certainty. 12 Q. What's your understanding, your 13 best understanding? 14 A. My understanding is that Joe, 15 since he -- in the validation report it 16 indicated to have tentative specification 17 limits for the control sera, that I would 18 provide additional control serum results 19 periodically to increase that number and allow 20 him to reassess the -- whether the control 21 limits were appropriate. 22 MR. KELLER: Let me mark two 23 exhibits. 24 - - - 25 (Exhibit Krah-39, 2/22/01 Fax,</p>	<p style="text-align: right;">Page 385</p> <p>1 Q. And here there's a listing of 44 2 assays. Do you see that? There's a reference 3 to -- the bottom right-hand corner says, "To 4 transfer 44 assays..."? 5 A. Yes. 6 MR. SANGIAMO: Object to the 7 form. 8 BY MR. KELLER: 9 Q. That's your handwriting. Correct? 10 A. Yes, it is. 11 Q. And here you're capturing for 44 12 assays that were run as part of Protocol 007 13 the mock averages for those 44 assays. Is 14 that a fair statement? 15 A. The mock value for those 44 16 assays. 17 Q. And it also references the low 18 and high controls for those assays as well? 19 MR. SANGIAMO: Object to the 20 form. 21 THE WITNESS: The two controls, 22 I don't recall that they were referred 23 to as high and low, but they are the 24 two controls that were run in the -- 25 BY MR. KELLER:</p>

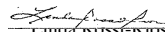
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<p style="text-align: right;">Page 386</p> <p>1 Q. You also --</p> <p>2 MR. SANGIAMO: Jeff, I shouldn't</p> <p>3 have to enforce Dr. Krah's right to</p> <p>4 finish his answers.</p> <p>5 BY MR. KELLER:</p> <p>6 Q. Are you done?</p> <p>7 A. The control sera that were used</p> <p>8 in each of the assays, adult lab volunteer</p> <p>9 control sera.</p> <p>10 Q. There is a chart that you</p> <p>11 provided. Can you -- it says number -- I</p> <p>12 can't quite read your handwriting.</p> <p>13 A. Number of assays at titer.</p> <p>14 Q. What are you trying to convey in</p> <p>15 this reference here?</p> <p>16 A. My -- or I can't say with</p> <p>17 certainty at the time what I was conveying,</p> <p>18 but I can say what I have there, which is a</p> <p>19 distribution of how many assays. For example,</p> <p>20 the MKY serum was providing a titer of 1,024</p> <p>21 versus 2,048, down to 512 at the far</p> <p>22 right-hand column. And then for the CM serum,</p> <p>23 the titers in -- how many times a serum had a</p> <p>24 given titer in an assay.</p> <p>25 Q. Is it fair to say that Joe</p>	<p style="text-align: right;">Page 388</p> <p>1 Q. And each assay that's run has a</p> <p>2 mock control limit, an N2 positive control</p> <p>3 limit that are run in that assay. Correct?</p> <p>4 MR. SANGIAMO: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: Each assay has a</p> <p>7 mock N2 positive control samples that</p> <p>8 are run. Each of which has limits for</p> <p>9 a valid assay.</p> <p>10 BY MR. KELLER:</p> <p>11 Q. So based on your review of the</p> <p>12 44 assays that you captured the MKY controls,</p> <p>13 was the MKY control performing consistently</p> <p>14 throughout these 44 assays, based on your</p> <p>15 opinion?</p> <p>16 A. Not being a statistician, I</p> <p>17 can't comment with statistical certainty, but</p> <p>18 I'd say 39 of the assays that had one titer of</p> <p>19 1,024, six times it was within a twofold range</p> <p>20 of that. And in one case it was five --</p> <p>21 sorry, two cases it was 512, which is twofold</p> <p>22 lower than 1,024.</p> <p>23 Q. Do you recall ever providing Joe</p> <p>24 Antonello before you finalized his validation</p> <p>25 report all the data from Protocol 007</p>
<p style="text-align: right;">Page 387</p> <p>1 Antonello was using the data generated during</p> <p>2 the Protocol 007 clinical runs to establish</p> <p>3 control runs?</p> <p>4 MR. SANGIAMO: Object to the</p> <p>5 form.</p> <p>6 THE WITNESS: Control -- my</p> <p>7 understanding is that the control,</p> <p>8 tentative control runs were set based</p> <p>9 on the validation protocol. Validation</p> <p>10 protocol indicated that additional</p> <p>11 assays would be run to gather</p> <p>12 additional data to verify or further</p> <p>13 support the control limit titers.</p> <p>14 These results are adult lab volunteer</p> <p>15 sera and the mocks that are</p> <p>16 involving -- they're from assays that</p> <p>17 involve Protocol 007 sera but these are</p> <p>18 not results related to Protocol 007</p> <p>19 samples.</p> <p>20 BY MR. KELLER:</p> <p>21 Q. But they're run, each one of</p> <p>22 these assays runs a paired sera from kids in</p> <p>23 Protocol 007. Correct?</p> <p>24 A. Each assay does, the data that</p> <p>25 were provided do not include those results.</p>	<p style="text-align: right;">Page 389</p> <p>1 including the serum runs?</p> <p>2 MR. SANGIAMO: Object to the</p> <p>3 form.</p> <p>4 THE WITNESS: I don't recall</p> <p>5 which, if any of the Protocol 007, the</p> <p>6 mocks N2 and adult lab volunteer</p> <p>7 control sera from -- that were included</p> <p>8 in Protocol 007 were provided to Joe.</p> <p>9 BY MR. KELLER:</p> <p>10 Q. Let me direct your attention to</p> <p>11 490656 which is on February 26, 2001. Let me</p> <p>12 know when you're there. If you look in the</p> <p>13 middle of the page under "Transferred," can</p> <p>14 you read what you wrote in your journal?</p> <p>15 A. It says, "Transferred Excel</p> <p>16 files to Joe Antonello and Robin from Protocol</p> <p>17 007 data summaries and the raw data files (44</p> <p>18 files each.)"</p> <p>19 Q. And those 44 files, are those</p> <p>20 the same 44 assays that you faxed to him, list</p> <p>21 the controls -- the control data?</p> <p>22 A. It's the same number of samples.</p> <p>23 I can't say with certainty that it's the same</p> <p>24 sample. It's the same number of assays.</p> <p>25 Q. Why did you provide Joe</p>

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<p style="text-align: right;">Page 390</p> <p>1 Antonello the raw data from Protocol 006 2 before -- at this time frame? Why did you do 3 that? 4 MR. SANGIAMO: Object to the 5 form. Are you going to let him read 6 the rest of it? 7 BY MR. KELLER: 8 Q. Strike that. 9 Dr. KraH, why did you provide 10 Joe Antonello on February 26th all the raw 11 data from Protocol 007? 12 MR. SANGIAMO: Feel free to read 13 the rest of the entry, Dr. KraH. 14 THE WITNESS: I can't recall. 15 Certainly I can read what it says, that 16 they would -- this was that "They will 17 apply the extravariability criteria 18 test" to the data. 19 BY MR. KELLER: 20 Q. Do you know whether or not Joe 21 Antonello used any of the data you used to 22 validate Protocol 007 to add information to 23 those 20 runs -- 24 MR. SANGIAMO: Object to the 25 form.</p>	<p style="text-align: right;">Page 392</p> <p>1 serum, the MKY and CM control limit 2 titers, from my interpretation, was the 3 only way to generate additional -- or 4 any way to generate additional data 5 would be using data from the actual 6 Protocol 007 testing. So my 7 expectation was when there was a 8 request to have data from additional 9 assays, the Protocol 007 assays would 10 be the source of those control limits 11 to include. 12 BY MR. KELLER: 13 Q. You testified earlier that you 14 didn't expect that those tentative runs would 15 be run with sera from Protocol 007 or run 16 through -- the assays run through Protocol 007 17 but would be run separately through different 18 assays? 19 MR. SANGIAMO: Objection. 20 Mischaracterizes testimony. 21 BY MR. KELLER: 22 Q. You didn't testify to that? 23 A. Not -- that's not what I believe 24 I testified to. 25 Q. Let me have you go back to</p>
<p style="text-align: right;">Page 391</p> <p>1 BY MR. KELLER: 2 Q. -- that were requested as part 3 of the protocol that were tentative? 4 MR. SANGIAMO: Object to the 5 form. 6 MR. KELLER: Let me strike that. 7 BY MR. KELLER: 8 Q. Could one of the reasons that 9 you provided the raw data to Joe Antonello to 10 help him update those tentative results with 11 more information to finalize the validation 12 report? 13 A. I don't recall that it was 14 related to the validation report. 15 Q. Do you know when the validation 16 report was finalized? 17 A. I don't recall. 18 Q. You don't recall. Did you ever 19 disclose to CBER that you provided Joe 20 Antonello data from the Protocol 007 runs to 21 help validate the AIGENT SOP? 22 MR. SANGIAMO: Object to the 23 form. 24 THE WITNESS: The control -- 25 providing to Joe the mock and control</p>	<p style="text-align: right;">Page 393</p> <p>1 Exhibit 38, which is your e-mail dated 2 December 10, 2001. Exhibit 38. You've read 3 this e-mail already. Correct? 4 A. Yes. 5 Q. In the second paragraph you 6 write, "The pediatric serum sample panels 7 (sets 8 and 5 from Bev Rich's group) were used 8 to evaluate seroconversion rates, 9 pre-positivity and the assay cutoff (titer of 10 32 assigned negative)." 11 Do you see that? 12 A. Yes. 13 Q. And those pediatric serum 14 panels, those are the ones that where 15 Antonello proposed running 100 paired sample 16 and you ultimately only had 50 paired sample. 17 Correct? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: I can't -- from 21 this, reading this, I can't tell how 22 many samples were in those sets. 23 BY MR. KELLER: 24 Q. I see. You go on to write, "As 25 recommended by Biometrics Research, the limits</p>

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<p style="text-align: right;">Page 394</p> <p>1 were re-evaluated after interim analysis set 2 was run to use a larger data set to establish 3 the limits (I believe they recommended 4 re-evaluating after 20 runs, since the number 5 of runs in the validation studies were too low 6 to provide an evaluation of the limits to be 7 set for these)." 8 Do you see that? 9 A. Yes. 10 Q. And so -- and that is -- is that 11 your understanding why you provided Joe 12 Antonello the results of running the controls 13 in Protocol 007 assays to help provide 14 sufficient data to set reliable controls? 15 MR. SANGIAMO: Object to the 16 form. Dr. KraH, you should feel free 17 to read the parts of the paragraph that 18 Mr. Keller elected to skip. 19 THE WITNESS: I believe, as 20 instructed, that the 20 runs that we 21 had, it indicates that the number of 22 runs in the validation study was too 23 low to provide an evaluation of the 24 limits for those. 25 BY MR. KELLER:</p>	<p style="text-align: right;">Page 396</p> <p>1 sufficiently large number of runs, 2 control serum values from assays that 3 were run as part of Protocol 007 were 4 included in that analysis. 5 MR. SANGIAMO: I got a feeling 6 we're pretty much right at seven hours. 7 I think we got five minutes. 8 VIDEOGRAPHER: Yeah. About two 9 minutes. 10 MR. KELLER: We're at our 11 seven-hour limit, Dr. KraH. Thank you 12 for your time. 13 VIDEOGRAPHER: The time is now 14 6:14. This concludes the video 15 deposition. 16 - - - 17 (Witness excused.) 18 - - - 19 (Deposition concluded at 20 6:14 p.m.) 21 22 23 24 25</p>
<p style="text-align: right;">Page 395</p> <p>1 Q. It's your testimony that those 2 20 runs were run in the assays that were used 3 in Protocol 007. Correct? 4 A. The 20, I'm sorry. 5 Q. The 20 runs to validate the 6 control limits were run through running the 7 assays in Protocol 007? 8 A. My understanding and 9 recollection is that those 20 runs are assay 10 runs as part of the validation and not from 11 Protocol 007. 12 Q. So is it your testimony that 13 when -- in the validation protocol you stated 14 that these results were tentative and that 20 15 more runs needed to be run, that those in 16 order to validate the protocol with sufficient 17 enough reliable data, that you had to look to 18 the running of the Protocol 007 data to get 19 sufficient data to have reliable data for the 20 controls? 21 MR. SANGIAMO: Object to the 22 form. 23 THE WITNESS: In order to -- my 24 understanding is in order to get the 25 data from a large enough or</p>	<p style="text-align: right;">Page 397</p> <p>1 CERTIFICATE 2 3 4 I do hereby certify that I am a Notary 5 Public in good standing, that the aforesaid 6 testimony was taken before me, pursuant to 7 notice, at the time and place indicated; that 8 said deponent was by me duly sworn to tell the 9 truth, the whole truth, and nothing but the 10 truth; that the testimony of said deponent was 11 correctly recorded in machine shorthand by me 12 and thereafter transcribed under my 13 supervision with computer-aided transcription; 14 that the deposition is a true and correct 15 record of the testimony given by the witness; 16 and that I am neither of counsel nor kin to 17 any party in said action, nor interested in 18 the outcome thereof. 19 20 WITNESS my hand and official seal this 21 20th day of July, 2017. 22 23 24 25</p> <p style="text-align: center;">  Linda Kossifricios, RPR, CSR Notary Public </p>

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<p style="text-align: right;">Page 398</p> <p>1 INSTRUCTIONS TO WITNESS</p> <p>2 Please read your deposition over</p> <p>3 carefully and make any necessary corrections.</p> <p>4 You should state the reason in the appropriate</p> <p>5 space on the errata sheet for any corrections</p> <p>6 that are made.</p> <p>7 After doing so, please sign the errata</p> <p>8 sheet and date it.</p> <p>9 You are signing same subject to the</p> <p>10 changes you have noted on the errata sheet,</p> <p>11 which will be attached to your deposition.</p> <p>12 It is imperative that you return the</p> <p>13 original errata sheet to the deposing attorney</p> <p>14 within thirty (30) days of receipt of the</p> <p>15 deposition transcript by you. If you fail to</p> <p>16 do so, the deposition transcript may be deemed</p> <p>17 to be accurate and may be used in court.</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 400</p> <p>1 ERRATA SHEET</p> <p>2 IN RE: USA ex rel. vs. MERCK</p> <p>3 DATE: 7/11/2017</p> <p>4 PAGE LINE CORRECTION AND REASON</p> <p>5 _____</p> <p>6 _____</p> <p>7 _____</p> <p>8 _____</p> <p>9 _____</p> <p>10 _____</p> <p>11 _____</p> <p>12 _____</p> <p>13 _____</p> <p>14 _____</p> <p>15 _____</p> <p>16 _____</p> <p>17 _____</p> <p>18 _____</p> <p>19 _____</p> <p>20 _____</p> <p>21 _____</p> <p>22 _____</p> <p>23 _____</p> <p>24 _____</p> <p>25 (DATE) DAVID KRAH</p>
<p style="text-align: right;">Page 399</p> <p>1 ACKNOWLEDGMENT OF DEPONENT</p> <p>2</p> <p>3 I have read the foregoing transcript of</p> <p>4 my deposition and except for any corrections or</p> <p>5 changes noted on the errata sheet, I hereby</p> <p>6 subscribe to the transcript as an accurate record</p> <p>7 of the statements made by me.</p> <p>8</p> <p>9 _____</p> <p>10 DAVID KRAH</p> <p>11</p> <p>12 SUBSCRIBED AND SWORN before and to me</p> <p>13 this ____ day of _____, 20__.</p> <p>14</p> <p>15</p> <p>16 _____</p> <p>17 NOTARY PUBLIC</p> <p>18</p> <p>19</p> <p>20 My Commission expires:</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>	

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IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

UNITED STATES OF AMERICA : CIVIL ACTION
ex rel., STEPHEN A. : NO. 2:10-04374 (CDJ)
KRAHLING and JOAN A. :
WLOCHOWSKI, :
Plaintiffs, :
vs. :
MERCK & CO., INC., :
Defendant. :

: Master File No.

IN RE: MERCK MUMPS : 2:12-cv-03555 (CDJ)
VACCINE ANTITRUST :
LITIGATION :

THIS DOCUMENT RELATES TO: :
ALL ACTIONS :

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July 12, 2017

Continued videotaped deposition of
DAVID KRAH, taken at the offices of Spector
Roseman & Kodroff, 1818 Market Street, Suite
2500, Philadelphia, Pennsylvania 19103,
beginning at 9:05 a.m., before LINDA
ROSSI-RIOS, a Federally Approved RPR, CCR and
Notary Public.

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<p style="text-align: right;">Page 402</p> <p>1 A P P E A R A N C E S :</p> <p>2</p> <p>3 On behalf of the Private Payor Plaintiffs</p> <p>4 SPECTOR ROSEMAN & KODROFF, P.C. BY: JOHN A. MACORETTA, ESQUIRE</p> <p>5 and DIANA J. ZINSER, ESQUIRE</p> <p>6 1818 Market Street Suite 2500 Philadelphia, PA 19103 215.496.0300</p> <p>8 jmacoretta@srkw-law.com dzins@srkw-law.com</p> <p>9</p> <p>10</p> <p>11 On behalf of the Relators</p> <p>12 CONSTANTINE CANNON LLP BY: GORDON SCHNELL, ESQUIRE and DANIEL VITELLI, ESQUIRE</p> <p>13 335 Madison Avenue New York, NY 10017 212-350-2700</p> <p>15 gschnell@constantinecannon.com dvitelli@constantinecannon.com</p> <p>16</p> <p>17</p> <p>18 On behalf of the Relators</p> <p>19 KELLER GROVER LLP BY: JEFFREY F. KELLER, ESQUIRE KATHLEEN R. SCANLAN, ESQUIRE and SARAH WYSOCKI, ESQUIRE</p> <p>21 1965 Market Street San Francisco, CA 94103 415.964.2939</p> <p>22 jfkeller@kellergrover.com kscanlan@kellergrover.com swysocki@kellergrover.com</p> <p>23</p> <p>24</p> <p>25</p>	<p style="text-align: right;">Page 404</p> <p>1 I N D E X</p> <p>2</p> <p>3 WITNESS PAGE</p> <p>4 DAVID KRAH</p> <p>5 By Mr. Schnell 406</p> <p>6</p> <p>7 E X H I B I T S</p> <p>8 MARKED DESCRIPTION PAGE</p> <p>9 Krah-40 8/7/01 E-mail with 525 attachment, 52249 - 52253</p> <p>10</p> <p>11 Krah-41 Summary of findings, 583 2021754 - 2021761</p> <p>12 Krah-42 2/20/01 Memo, 616 26443 & 26444</p> <p>13</p> <p>14 Krah-43 6/21/01 Memo, 632 63805</p> <p>15 Krah-44 7/30/01 Memo, 644 00002211 - 00002230</p> <p>16</p> <p>17 Krah-45 Counting sheets, 657 00683926 - 00683930</p> <p>18 Krah-46 Counting sheets, 657 00683514 - 00683518</p> <p>19</p> <p>20 Krah-47 Series of e-mails, 668 00026555 - 00026559</p> <p>21 Krah-48 Spreadsheet, 668 00050333 - 00050342</p> <p>22</p> <p>23 Krah-49 8/1/01 Memo, 679 00026864</p> <p>24 Krah-50 007 Summary, 686 00054460</p> <p>25</p>
<p style="text-align: right;">Page 403</p> <p>1 A P P E A R A N C E S (cont'd.):</p> <p>2</p> <p>3</p> <p>4 On behalf of the Defendant, Merck & Co., Inc.</p> <p>5 MORGAN LEWIS & BOCKIUS LLP BY: LISA C. DYKSTRA, ESQUIRE</p> <p>6 1701 Market Street Philadelphia, PA 19103 215-963-5000</p> <p>7 ldykstra@morganlewis.com</p> <p>8</p> <p>9</p> <p>10 On behalf of the Defendant, Merck & Co., Inc. and the Witness</p> <p>11 VENABLE LLP BY: DINO S. SANGIAMO, ESQUIRE and SALLY W. BRYAN, ESQUIRE</p> <p>12 750 East Pratt Street Suite 900 Baltimore, MD 21202 410-244-7400</p> <p>14 dssangiamo@venable.com srbryan@venable.com</p> <p>15</p> <p>16</p> <p>17 A L S O P R E S E N T :</p> <p>18</p> <p>19 TIMOTHY K. HOWARD, ESQUIRE TINA BARTON, ESQUIRE Merck in-house counsel</p> <p>20</p> <p>21 STEPHEN A. KRAHLING</p> <p>22</p> <p>23 JOAN A. WLOCHOWSKI</p> <p>24</p> <p>25 DANIEL GRBICH, Videographer</p> <p>- - -</p>	<p style="text-align: right;">Page 405</p> <p>1 E X H I B I T S (cont'd.)</p> <p>2 Krah-51 9/21/00 Memo, 688 00014572 - 00014575</p> <p>3</p> <p>4 Krah-52 8/15/00 E-mail, 694 00068546</p> <p>5 Krah-54 Collection of papers, 702 00064825 - 00064831</p> <p>6</p> <p>7 Krah-55 Test result, 707 00069449</p> <p>8 Krah-56 10/9/00 Memo with 718 attachment, 00065695 - 00065703</p> <p>9</p> <p>10 Krah-57 3/29/01 Memo, 727 00015702 & 00015703</p> <p>11</p> <p>12 Krah-58 6/18/01 E-mail, 729 00048555</p> <p>13 Krah-59 6/20/01 E-mail, 733 00048558</p> <p>14</p> <p>15</p> <p>16</p> <p>17</p> <p>18</p> <p>19</p> <p>20</p> <p>21</p> <p>22</p> <p>23</p> <p>24</p> <p>25</p>

2 (Pages 402 - 405)

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1 - - -
 2 VIDEOGRAPHER: The date today is
 3 July 12, 2017. The time is
 4 approximately 9:05. This begins disc
 5 one of the continuation deposition of
 6 David Krah. You may proceed.
 7 - - -
 8 DAVID KRAH, after having been
 9 previously duly sworn, was examined and
 10 testified as follows:
 11 - - -
 12 EXAMINATION
 13 - - -
 14 BY MR. SCHNELL:
 15 Q. Good morning, Dr. Krah.
 16 A. Good morning.
 17 Q. As I introduced myself, I'm
 18 Gordon Schnell and I'm going to be asking you
 19 questions today.
 20 A. Okay.
 21 Q. In your opinion -- well, let
 22 me -- let's get the record straight because I
 23 want to make sure we understand what the
 24 AIGENT test is. We got it yesterday. It's
 25 spelled A-I-G-E-N-T. Correct, Dr. Krah?

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1 A. That's the acronym that we use
 2 for it, yes.
 3 Q. And that stands for anti-IgG
 4 enhanced neutralization test. Right?
 5 A. Yes.
 6 Q. In your opinion, was the AIGENT
 7 test a reliable test?
 8 A. In my opinion it met the
 9 appropriate criteria that were set in the
 10 validation plan, and as such, would be a
 11 reliable assay.
 12 Q. And it was a reliable assay, in
 13 your opinion, for what purpose?
 14 A. It was a reliable assay for the
 15 purpose of testing human sera for mumps
 16 neutralizing activity.
 17 Q. Was it a reliable test for
 18 measuring the immunogenicity of the mumps
 19 component of MMR II?
 20 A. I would say it was a reliable
 21 test to measure antibody to mumps. As such,
 22 the measurement of -- our intention was to use
 23 the antibody measurement as a means to assess
 24 the immunogenicity of the mumps component of
 25 MMR.

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1 Q. That wasn't my question.
 2 MR. SCHNELL: Can you repeat my
 3 question, please?
 4 - - -
 5 (The court reporter read the
 6 pertinent part of the record.)
 7 - - -
 8 MR. SANGIAMO: Object to the
 9 statement. Object to the implication
 10 that he hasn't answered the question,
 11 but you're asking that question again?
 12 MR. SCHNELL: Could you just
 13 object to form and leave the coaching
 14 out, please.
 15 MR. SANGIAMO: I'm not coaching.
 16 I will make the objections that are
 17 appropriate.
 18 MR. SCHNELL: Are you objecting
 19 to form?
 20 MR. SANGIAMO: Are you asking
 21 that question again?
 22 MR. SCHNELL: I am asking that
 23 question again. Please limit the
 24 objection --
 25 MR. SANGIAMO: Then I object.

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1 MR. SCHNELL: -- to object to
 2 the form.
 3 MR. SANGIAMO: I'll object
 4 consistent with the way objections are
 5 supposed to be made.
 6 THE WITNESS: I would say it
 7 was, in my view, a reliable test to
 8 measure antibody. If antibody
 9 measurement was -- as antibody with the
 10 criteria that antibody measurement in
 11 the neutralization assay was an
 12 assessment of immunogenicity, I would
 13 say it was a reliable measure of
 14 immunogenicity.
 15 BY MR. SCHNELL:
 16 Q. And was the antibody assessment
 17 an accurate measure of immunogenicity?
 18 MR. SANGIAMO: Object to the
 19 form.
 20 THE WITNESS: I would say the --
 21 all I can say is that the assay in my
 22 view was a reliable assay to measure
 23 antibody. If antibody is the criteria
 24 measure of immunogenicity, then the
 25 assay was reliable and suitable to be

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1 able to measure the immunogenicity.
 2 BY MR. SCHNELL:
 3 Q. I'm asking, is the antibodies
 4 that were measured in your AIGENT test an
 5 accurate measure of immunogenicity of the
 6 mumps component of MMR II?
 7 MR. SANGIAMO: Object to the
 8 form. Asked and answered.
 9 THE WITNESS: It was an assay
 10 format that was agreed to in discussion
 11 with CBER as a means to measure
 12 antibody responses to measles -- to
 13 measles, I'm sorry. To mumps.
 14 MR. SCHNELL: Can you, please,
 15 repeat my question?
 16 - - -
 17 (The court reporter read the
 18 pertinent part of the record.)
 19 - - -
 20 THE WITNESS: I would say the
 21 assay, in my view, was a reliable
 22 assay. The measurement endpoint of
 23 measuring antibodies with the AIGENT
 24 assay was discussed and agreed to in
 25 collaboration with CBER. So given

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1 those statements, the expectation would
 2 be that it was a reliable measure of
 3 immunogenicity to mumps.
 4 BY MR. SCHNELL:
 5 Q. Do you believe it was an
 6 accurate measure of immunogenicity?
 7 A. That's beyond my scope of
 8 responsibility and training. I can speak to
 9 the assay performance itself, not to the
 10 clinical implications.
 11 Q. That's what I'm asking. In your
 12 opinion, did your assay give a reliable
 13 measure of the immunogenicity of the mumps
 14 component of MMR II?
 15 MR. SANGIAMO: Objection. Asked
 16 and answered.
 17 THE WITNESS: That's beyond the
 18 scope of my responsibility and
 19 training.
 20 BY MR. SCHNELL:
 21 Q. So your testimony is you don't
 22 have an opinion one way or another whether the
 23 AIGENT assay is an accurate measure of the
 24 immunogenicity of the mumps component of
 25 MMR II?

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1 MR. SANGIAMO: Objection. Asked
 2 and answered.
 3 THE WITNESS: I have an opinion
 4 that the assay was reliable in
 5 measuring antibodies to mumps. As far
 6 as the impact on -- or the conclusion
 7 about whether it was reliable
 8 assessment to immunogenicity, I can't
 9 say.
 10 BY MR. SCHNELL:
 11 Q. Do you have an opinion as to
 12 whether or not the AIGENT assay was a reliable
 13 measure of how well the mumps component of
 14 MMR II protects vaccine recipients from
 15 getting the mumps disease?
 16 A. I don't have any opinion on
 17 that.
 18 Q. Do you have an opinion on how
 19 well the mumps component of MMR II works today
 20 in protecting vaccine recipients from
 21 contracting mumps?
 22 A. I don't have an opinion on that.
 23 Q. You have no idea?
 24 MR. SANGIAMO: Object to the
 25 form.

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1 THE WITNESS: I read reports and
 2 taken part in meetings discussing
 3 protection from mumps, but I have no
 4 independent knowledge of -- or no
 5 independent opinion other than what
 6 I've read or discussed in meetings.
 7 BY MR. SCHNELL:
 8 Q. And all the clinical testing
 9 that you did while at Merck on the mumps
 10 component of MMR II has given you no
 11 indication one way or another as to how well
 12 the vaccine works at protecting vaccine
 13 recipients from contracting mumps?
 14 MR. SANGIAMO: Objection. Asked
 15 and answered.
 16 THE WITNESS: That's correct,
 17 none of the work -- the work that I did
 18 was involved in the assay development
 19 and using the assay, not in connecting
 20 those results to project on how well
 21 the mumps component works.
 22 BY MR. SCHNELL:
 23 Q. In terms of the data that
 24 resulted from the AIGENT test, is it your
 25 opinion that the data was reliable?

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1 A. Yes.

2 Q. And there were two sets of data

3 that came out of the AIGENT testing. There

4 was what Merck has described as,

5 quote/unquote, original data, and what Merck

6 has described as, quote/unquote, corrected

7 data. Is that true?

8 MR. SANGIAMO: Object to the

9 form.

10 THE WITNESS: Could you clarify

11 what you mean by came out of Merck? I

12 believe you said data that came out of

13 Merck.

14 BY MR. SCHNELL:

15 Q. I don't know if I said that, but

16 have you heard of the term "original data and

17 corrected data" as it relates to AIGENT -- the

18 AIGENT study results?

19 MR. SANGIAMO: Object to the

20 form.

21 THE WITNESS: To the data -- I

22 do recall hearing those terms used in

23 connection with the data.

24 BY MR. SCHNELL:

25 Q. What's your understanding of

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1 what, quote/unquote, original data means in

2 that context?

3 A. My understanding of that term is

4 that those are the plaque counts as

5 recorded -- as the primary data recorded in

6 counting the plaques.

7 Q. What do you mean "primary data"?

8 A. The first -- the data that the

9 person counting the assay recorded first.

10 Q. And then what's your

11 understanding of what, quote/unquote,

12 corrected data means as it relates to the

13 AIGENT study results?

14 A. My understanding of the

15 corrected data, those are values that had been

16 changed from whatever the original entry was.

17 Q. And if an original data point

18 was changed to become a corrected data point,

19 and then it was changed again, would you

20 consider that still corrected?

21 A. I would consider anything beyond

22 the original entry as a corrected value.

23 Q. And if an original data point

24 was changed so it became corrected but then it

25 was changed again back to the original data

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1 point, would you consider that original or

2 corrected data?

3 A. My view of the original data was

4 whatever the first number that was written

5 down was for the plaque count. So if -- I

6 would still consider that -- it's a number

7 that's -- gets into semantic argument. The

8 number would be a -- I would say it's a

9 corrected number, but it's the same as the

10 original -- in that description, as I

11 understood it, it's the same as the original

12 number.

13 Q. In your earlier answer when you

14 testified that in your opinion the AIGENT data

15 was reliable, were you referring to both the

16 original data and the corrected data?

17 A. Yes.

18 Q. Do you have an opinion one way

19 or another as to which, if either, of the sets

20 of data was more reliable than the other?

21 A. I have an opinion based on

22 analysis that our -- I don't recall if it was

23 the biometrics group or another group did at

24 Merck comparing corrected data with the

25 original data.

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1 Q. And what's your opinion based on

2 that?

3 A. That the -- both results are

4 comparable.

5 Q. In terms of what?

6 A. Seroconversion rate, as best I

7 recall.

8 Q. What about in terms of

9 pre-positive rates?

10 A. That, I don't recall what

11 difference there was between the groups.

12 Q. What about in terms of invalid

13 assays?

14 A. That, I don't recall.

15 Q. So, again, is your opinion that

16 both sets of data are equally reliable?

17 A. Yes.

18 Q. So you don't believe the

19 corrected data is more reliable than the

20 original data for the purposes of the AIGENT

21 test?

22 A. In looking at the global

23 compiled data, I feel that they're both --

24 they both gave comparable seroconversion

25 rates. Both are comparable estimates of

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1 providing data that are equally usable.
 2 Q. Equally usable for what?
 3 A. For assessing seroconversion
 4 rate.
 5 Q. What about for assessing the
 6 reliability of the AIGENT test, do you have an
 7 opinion one way or another as to which was the
 8 better set of data if one was indeed better
 9 than the other in your view?
 10 MR. SANGIAMO: Object to the
 11 form.
 12 THE WITNESS: I don't have an
 13 opinion on that.
 14 BY MR. SCHNELL:
 15 Q. I want you to take me through
 16 the process in your lab that occurred with the
 17 AIGENT testing as it related to the counting
 18 of plaques. So could you kind of give me the
 19 narrative of call it a flow as to what your
 20 lab staff and you did in trying to calculate
 21 plaque counts from the various assays that
 22 were being tested in the AIGENT?
 23 A. As best I can recall, the --
 24 start from the point where the plates are
 25 stained and the plaques are visible, a counter

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1 would look at the plate typically with a light
 2 box to give some better visualization of the
 3 plaques, mark plaques with a Sharpie pen or an
 4 ink -- a laboratory ink pen, and then write
 5 the plaque count typically on the, could be
 6 the plate bottom or the plate lid. Different
 7 people had different preferences as to where
 8 to record the number. Those -- after an assay
 9 was counted, then those plaque counts would be
 10 transcribed into a notebook page which listed
 11 the plate number and then for each sample
 12 there are four -- sorry, three replicate
 13 wells, so it would be a spreadsheet capturing
 14 the plaque counts by plate and by replicate
 15 column row. Those plaque counts then would be
 16 transcribed into an Excel spreadsheet where a
 17 calculation would be done of the average
 18 number of plaques for the replicates and then
 19 a calculation of the plaque count as a percent
 20 of the mock value. And then an analyst would
 21 look at the data and assign a titer to the
 22 sample based on the highest serum dilution
 23 providing 50 percent or more neutralization.
 24 Q. Is that the total path of the
 25 counting process?

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1 A. They're all the steps that come
 2 to mind right now that capture the general
 3 flow, the flow.
 4 Q. Now, there was a correction log
 5 at some point that was instituted into this
 6 flow as well. Right?
 7 A. There were plaque count checks
 8 that were driven by observations from the
 9 workbook, meaning flags that -- it's different
 10 for the first third of the data versus the
 11 second third and the third third of the data;
 12 meaning that in the second third and the third
 13 third a workbook was available that was
 14 implemented or included flags for various
 15 criteria that were identified as -- some of
 16 them I recall being part of the validation
 17 plan. They would identify samples that were
 18 deemed or warranting a check to verify that
 19 the plaque counts were accurate.
 20 Q. That was only for the first
 21 third?
 22 A. I'm sorry. That was for the
 23 second third and the third third. For the
 24 first third we did not have that, a workbook
 25 that displayed flags identifying samples

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1 warranting every check to verify accuracy.
 2 Q. How did you check accuracy for
 3 the first third?
 4 A. As best I recall, some examples
 5 were looking for or screening -- looking
 6 through the data. Sample sera are tested at
 7 multiple dilutions. We identify sera that
 8 were positive at a single dilution. Another
 9 example would be if we had samples where
 10 the -- there was -- I'm trying to think of the
 11 term, inconsistent neutralization or erratic
 12 neutralization, meaning that it was jumping
 13 back and forth in multiple dilutions between
 14 positive and negative. And at least in one
 15 other example, if we saw -- or one of the
 16 validity criteria for the test was to have no
 17 plaques in the unaffected cell control. So if
 18 we had an assay where there were plaques in
 19 the unaffected cell control, we would verify
 20 that they were indeed plaques. I can't say
 21 that that's all of the criteria that we used
 22 at first, but at least those are the ones that
 23 come to mind.
 24 Q. So I want to make sure I
 25 understand this. So with the first third of

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<p style="text-align: right;">Page 422</p> <p>1 the data, and was that also referred to as the 2 preliminary subset analysis? 3 A. I recall it as an interim 4 analysis, but it may have had different 5 descriptions. 6 Q. You recall a term "interim 7 analysis," is that what you said? 8 A. That's the term that I'm 9 recalling. I don't know what the official, if 10 there was an official description of that 11 first third. 12 Q. Did I say it right, interim 13 analysis or was it interim subset analysis? 14 A. I can't recall with certainty, 15 but the phrase that's coming to mind is 16 interim analysis. But I can't say that's 17 the -- that is necessarily an official 18 description. 19 Q. What period of time did the 20 counting of plaques for the interim analysis 21 take place? 22 A. I don't recall specific dates, 23 but it would have been in the time frame of 24 when we were running assays for that first 25 third. As best I recall, it was towards the</p>	<p style="text-align: right;">Page 424</p> <p>1 to why you wanted an early read on the data? 2 A. I don't have a general -- I 3 don't have a recollection of the reason. The 4 only recollection I have was a discussion 5 we're getting -- having -- rather than waiting 6 till the full study is done, have a read into 7 the results from a subset of the data. I 8 don't recall the official reason for that. 9 Q. In the clinical trial work that 10 you've done at Merck over the last, it's been 11 about 30 years. Right? 12 A. I've been at Merck about 13 30 years. 14 Q. Yeah. In the clinical trial 15 work that you've done there, is it typical to 16 have an interim analysis done on the data that 17 you're testing? 18 MR. SANGIAMO: Object to the 19 form. 20 THE WITNESS: I can't say that 21 it's typical. In other studies that 22 I've been involved in, it's one other 23 study, I don't recall there being an 24 interim analysis. 25 BY MR. SCHNELL:</p>
<p style="text-align: right;">Page 423</p> <p>1 end of 2000. I don't recall -- and into the 2 early part, meaning, as best I can recall, the 3 first quarter of 2001. 4 Q. So does November 2000 to 5 February of 2001 sound about right? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: I don't recall. I 9 only recall it was late 2000 into the 10 first quarter of 2001. 11 BY MR. SCHNELL: 12 Q. So let's talk about that period 13 of time and the counting that was done for the 14 interim analysis. By the way, why was there 15 an interim analysis done? 16 A. I don't have a full understanding 17 of the reason for it. I have a general 18 understanding. I don't know if that's the 19 official reason. My general understanding is 20 that it was to provide an analysis of an 21 earlier read on the results of the 22 immunogenicity testing for Protocol 007 before 23 waiting till we had the full testing for the 24 full set done. 25 Q. And what's your understanding as</p>	<p style="text-align: right;">Page 425</p> <p>1 Q. You've only been involved in one 2 other study at your time at Merck? 3 A. One other clinical study that I 4 can recall. 5 Q. Is that Protocol 006? 6 A. Yes. 7 Q. Those are the only two clinical 8 studies that you've been involved in at your 9 30 years at Merck? 10 A. As best I can recall, yes, as 11 far as running antibody assays, or any assays. 12 Q. What was -- was there anything 13 special about Protocol 006 and Protocol 007 14 that led to you being tasked with running 15 those assays? 16 MR. SANGIAMO: Objection. 17 Answer if you know. 18 THE WITNESS: I'm not aware of 19 anything special about the studies. I 20 would offer that at least my manager 21 Alan Shaw approached our group to 22 develop the assays given our virology 23 expertise. 24 BY MR. SCHNELL: 25 Q. So going back to the interim</p>

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1 analysis which occurred, as you say, in late
 2 2000, towards the first quarter of 2001, who
 3 were, during that period, the staff members in
 4 your lab who were involved in counting?
 5 A. I can't say certainly who all of
 6 them were. We had -- there were some
 7 personnel changes during that time, so I would
 8 not be able to recite all of the people who
 9 might have been involved in the counting.
 10 Q. Can you tell me who you do
 11 recall?
 12 A. At least some of the assays
 13 would have included myself, Mary Yagodich,
 14 Colleen Barr. I believe some with Elizabeth
 15 Thoryk. I expect there are two other people,
 16 Stephen Krahling and Joan Wlochowski were in
 17 the lab in the first quarter. I don't
 18 recall -- I expect that there would be assays
 19 that they counted. I don't recall that with
 20 certainty.
 21 Q. You didn't mention Jennifer
 22 Kriss, was she one of the ones also?
 23 A. Jennifer Kriss was in the lab.
 24 I expect that she would have been one of the
 25 counters. I expect that she would be. I

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1 can't say with certainty that she was one, but
 2 I expect that she would have been one.
 3 Q. Any others you can recall?
 4 A. None that come to mind.
 5 Q. In your opinion, were there any
 6 individuals within that group, including you,
 7 who were better at counting than others?
 8 A. To my understanding, the best of
 9 my recollection, each of the counters was
 10 compared to a -- their counting accuracy was
 11 compared against a reference counter. So
 12 there was a reference counter, but in the --
 13 as part of the training, the plaque
 14 counting -- as best I can recall, the plaque
 15 counting verification was done with a subset
 16 of plates from, I'll say, an assay. It may
 17 not be any particular study but just a set of
 18 plates that had plaques on them and to -- and
 19 verify that the new counters were counting
 20 within a targeted range of the reference
 21 counters.
 22 Q. And that was something that was
 23 done before the actual counting of plaques and
 24 the AIGENT study commenced?
 25 A. As best as I recall, that plaque

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1 counting training was done before any --
 2 before those individuals counted plaques
 3 independently.
 4 Q. So you wouldn't allow someone to
 5 count plaques unless they pass that
 6 preliminary test of counting ability. Is that
 7 correct?
 8 A. That's the best of my
 9 recollection, yes.
 10 Q. In the course of the counting,
 11 and now I'm extending it not only to the
 12 interim analysis but the full range of
 13 counting, were there any counters that you
 14 found particularly good or particularly bad?
 15 A. I did -- later in the year I did
 16 a review or a verification of plaque counts
 17 against all the counters in the lab. As best
 18 I recall, there was one counter who had some
 19 assays that were given beyond the 10 percent
 20 counting consistency target.
 21 Q. Just one?
 22 A. As best I recall it was just
 23 one.
 24 Q. Was that Mr. Krahling?
 25 A. Yes.

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1 Q. So what action, if any, did you
 2 take in response to that?
 3 A. I recall talking to Mr. Krahling
 4 about the plaque counts were identified as
 5 being extra variable, and asked him to be
 6 extra careful in counting plaques in
 7 subsequent assays.
 8 Q. So you didn't stop him from
 9 counting plaques?
 10 A. I don't recall that I stopped
 11 him, but I don't recall that he had any --
 12 that any other assays were counted by him
 13 after we had identified the plaque count
 14 accuracy question.
 15 Q. Who was the reference counter
 16 that you earlier testified about?
 17 MR. SANGIAMO: Object to the
 18 form.
 19 THE WITNESS: The reference
 20 counter that originally was established
 21 was Mary Yagodich.
 22 BY MR. SCHNELL:
 23 Q. Was that because you thought she
 24 was a highly qualify counter?
 25 A. That's because she was the

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<p style="text-align: right;">Page 430</p> <p>1 person in my view, who developed the assay and 2 was the most experienced person in running the 3 assay. 4 Q. Mary developed -- Mary Yagodich 5 developed the assay? 6 A. In collaboration with me and 7 others in the lab. 8 Q. Who else was involved in the 9 development of the assay? 10 A. I was -- there were others -- 11 there were other people in the lab who may 12 have contributed experiments. I don't recall 13 who -- I don't know who first was involved in 14 running any of the development experiments. 15 Q. But in terms of who came up with 16 the assay, that was you and Mary? 17 A. The assay was developed in 18 discussion with CBER as far as the assay 19 design and specifics including the virus 20 strain, use of anti-IgG, the endpoint, the 21 staining method. We had -- Mary and I and 22 others in the lab had done experiments to 23 evaluate effects of variables in the assay and 24 then relay that information to CBER to get a 25 consensus on the format for the assay.</p>	<p style="text-align: right;">Page 432</p> <p>1 third, and the assignment of a titer was no 2 different between the first third and the 3 second third and third third. The difference 4 was that in the second third and third third 5 there was a workbook that indicated flags for 6 various results being extra variability, 7 invalid dilution as examples. 8 Q. Let's look at that because you 9 also mentioned for the first third there 10 wasn't a flag system set up, but there was, I 11 think you described it as the counters looking 12 for certain things. Were the things -- you 13 gave a couple of examples. Before we go 14 through those examples, I want us -- were the 15 things that counters were looking for in the 16 first third of the AIGENT testing for accuracy 17 purposes ultimately incorporated into the 18 flagging system or was there a difference in 19 terms of measuring the accuracy between the 20 two portions of the AIGENT testing? 21 MR. SANGIAMO: Object to the 22 form. 23 BY MR. SCHNELL: 24 Q. Let me make this easier. So for 25 the first third when you I asked earlier about</p>
<p style="text-align: right;">Page 431</p> <p>1 Q. But in terms of who at Merck led 2 the design and development of the AIGENT test, 3 that was you and Mary. Correct? 4 A. To the best of my recollection, 5 yes. 6 Q. In terms of who led the testing, 7 the AIGENT testing, that was you. Correct? 8 A. I was in charge of the lab that 9 was running the AIGENT testing, the mumps 10 AIGENT testing. 11 Q. Was Mary Yagodich the only 12 reference counter in the AIGENT testing? 13 A. I was -- I considered myself a 14 reference counter as well. 15 Q. Anyone else? 16 A. I don't recall. I don't recall. 17 Q. So getting back to the flow of 18 the counting process, we'll start with the 19 interim analysis because you said it was 20 different for the first third of the AIGENT 21 test than it was for the second two-thirds. 22 Correct? 23 A. The analysis, the calculation of 24 percent of mock was no different. What was 25 different was the second third and the third</p>	<p style="text-align: right;">Page 433</p> <p>1 how you confirmed the accuracy of the 2 counting, you identified the counters would 3 look for data at a positive neutralization at 4 a single dilution? Correct? 5 A. Yes. 6 Q. And you also mentioned they 7 would look for erratic neutralizations. 8 Correct? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: That was an 12 example of a case where plates were 13 checked for accuracy. 14 BY MR. SCHNELL: 15 Q. But that was something that you 16 directed the counters to be looking for when 17 they were doing these counting for the first 18 third of the test? 19 A. I don't recall -- in some 20 cases -- so I don't recall necessarily 21 directing the counters to look for that in 22 each assay, but in some cases, I would review 23 the data and notice these conditions and then 24 relay that information to the counter. 25 Q. And is that the same for the</p>

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<p style="text-align: right;">Page 434</p> <p>1 positive neutralizations at a single dilution? 2 A. There are cases for the single 3 positive dilution where I relayed that 4 information to the original counter. 5 Q. Is that the same for the plaques 6 in the unaffected cell control plate? 7 A. Yes. 8 Q. Were there -- other than those 9 three items, and, again, that's positive 10 neutralization a single dilution, erratic 11 neutralization or plaques in unaffected cell 12 control plate, were there any other criteria 13 that you were looking for in these -- in the 14 interim analysis to ensure the accuracy of the 15 counts? 16 A. I do recall some other conditions. 17 I can't say that I recall each one of them. 18 One example is a sample that would have an 19 unexpected result, meaning, for example, 20 pre-positive but post-negative. 21 Pre-vaccination positive and post-vaccination 22 negative. 23 Q. That would be an example of -- 24 would that be an example of an unexpected 25 result?</p>	<p style="text-align: right;">Page 436</p> <p>1 looked at every single counting sheet for 2 these criteria to ensure accuracy of the data? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: As best I recall, 6 the reviews that were done with Emilio 7 Emini were going through, as best I 8 recall, each counting sheet. 9 BY MR. SCHNELL: 10 Q. So your testimony is Dr. Emini 11 reviewed every counting sheet in the interim 12 analysis? 13 A. I can't say for the full interim 14 analysis, but at least some number of assays 15 from the interim analysis. 16 Q. Was there any rhyme or reason as 17 to which assays he reviewed? 18 A. No. As best I can recall, they 19 were whatever assays were available at the 20 time. 21 Q. When he would review them, would 22 he come to the lab or you would bring them to 23 him? 24 A. I would bring them to him. 25 Q. He directed you to do that?</p>
<p style="text-align: right;">Page 435</p> <p>1 A. It would be an example of an 2 unexpected result with -- at least from my 3 best recollection a question of whether 4 there's a chance that the sera were reversed 5 in the assay inadvertently. 6 Q. Any other criteria you were 7 looking for to ensure accuracy with respect to 8 the interim analysis? 9 A. I believe there were others, but 10 I can't -- I don't recall others off the top 11 of my head. 12 Q. Now, for the first -- for the 13 interim analysis were you the only one who was 14 looking through the data for these types of 15 criteria to ensure accuracy? 16 A. No. 17 Q. Who else was looking through the 18 data? 19 A. Emilio Emini. 20 Q. Anyone else? 21 A. I don't recall. I can't exclude 22 anyone else, but I don't recall anyone else. 23 Q. And the process under which you 24 and Dr. Emini went through, was it a formal 25 process where you looked -- you or he or both</p>	<p style="text-align: right;">Page 437</p> <p>1 A. Yes. 2 Q. What about what you did during 3 the interim analysis, did you review every 4 counting sheet for these criteria to ensure 5 accuracy? 6 A. I recall at least looking 7 through each counting sheet for the single 8 positive dilution criteria. My best 9 recollection is that I applied the rules 10 uniformly across all the assays. So I would 11 say that each -- I did review each assay, each 12 counting sheet for those criteria. 13 Q. So in the instances where 14 Dr. Emini reviewed the -- are we calling them 15 counting sheets, is that the right term? 16 A. What actually is reviewed is not 17 the counting sheet but the Excel spreadsheet 18 where the counts are transcribed into. 19 Q. And that Excel spreadsheet would 20 contain what information? 21 A. That would contain a plate code, 22 the serum dilution, the plaque counts and 23 average number of counts and percent -- 24 average number of plaques and then a percent 25 of mock that correlates with that number of</p>

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1 plaques.
 2 Q. So it would have all the
 3 information you would need to calculate
 4 whether something was a pre- or post-positive
 5 or a pre- or post-negative. Correct?
 6 A. The counting sheet -- I'm sorry,
 7 not the counting sheet. The spreadsheet would
 8 not necessarily include the identification of
 9 which was a pre-vaccination or post-vaccination
 10 serum.
 11 Q. Isn't that -- the spreadsheet
 12 does not contain that information?
 13 A. At least the spreadsheet that we
 14 used for the first, as best I recall, we -- as
 15 best I recall, we wrote the -- I don't recall
 16 that the spreadsheet had -- as best I can
 17 recall, the spreadsheet had the plate code and
 18 the plaque counts and then we wrote, as best
 19 as I can recall, the serum identification in
 20 the right-hand column. So when the data was
 21 being reviewed with Emilio, I don't -- or --
 22 with Emilio, I don't recall whether that
 23 information was on the spreadsheet or not.
 24 Q. But didn't you say earlier that
 25 one of the criteria you looked for was whether

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1 there was a pre-positive and a post-negative?
 2 A. Yes.
 3 Q. So how would you be able to
 4 determine that if you didn't know which were
 5 the pres and which were the posts?
 6 A. Eventually we would assign a
 7 titer to those samples and compile the
 8 results. At that point we'd know which --
 9 what titer was corresponding to what pre- --
 10 the post-vaccination serum.
 11 Q. So for this review of accuracy
 12 you ultimately had all the information you
 13 needed to determine which was a pre- or
 14 post-positive or a pre- or post-negative.
 15 Correct?
 16 A. Ultimately that information
 17 was available. It doesn't necessarily follow
 18 that the review always included that final
 19 compilation that included those details.
 20 Q. Your review of the data did.
 21 Correct?
 22 A. Some of it did, not all of it.
 23 Q. So how did you determine whether
 24 you were going to do a complete review or a
 25 review that didn't have all the information

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1 you needed to identify the criteria you
 2 identified before for accuracy purposes?
 3 A. I'm sorry, you referenced a full
 4 review?
 5 Q. Well, a review that would enable
 6 you to look for positive neutralizations at a
 7 single dilution, erratic neutralizations,
 8 plaques in the unaffected cell control plate
 9 and whether a pre-positive went to a
 10 post-negative or other what you might describe
 11 as unexpected behavior?
 12 A. Often the first two of those,
 13 the single positive dilution or erratic
 14 neutralization could be viewed without knowing
 15 whether it's a pre-vaccination or
 16 post-vaccination serum just looking at the
 17 data in column form where you have dilutions
 18 of the sera and looking at the percentage of
 19 the neutralization across the dilutions of the
 20 sera. To do the assessment of, for example,
 21 pre-positive or post-negative or verify
 22 whether there were plaques in the unaffected
 23 cell control, at that point we would -- I
 24 would need the code to know what data cells
 25 corresponded with what plate code.

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1 Q. Sometimes you had information
 2 and sometimes you didn't?
 3 A. The data would be eventually
 4 available. I can't exclude that I didn't do
 5 review of the -- the single positive dilution
 6 or erratic neutralization before all that data
 7 was compiled.
 8 Q. Is it you don't recall? Is
 9 it -- I didn't understand your answer. You
 10 said you can't exclude --
 11 A. I can't exclude that there
 12 weren't cases that the data were -- the review
 13 of the single positive dilution and extra
 14 variability was assessed before doing the
 15 compilation of sera codes to go along with the
 16 samples.
 17 Q. So were there instances when
 18 after you delivered to Dr. Emini the
 19 spreadsheet pages that had the information you
 20 discussed on it, that he came back to you and
 21 said this looks questionable to me, have the
 22 counter go back and take a second look?
 23 MR. SANGIAMO: Object to the
 24 form.
 25 THE WITNESS: I do recall cases

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<p style="text-align: right;">Page 442</p> <p>1 reviewing the data with Emilio that he 2 did -- I would have particular 3 dilutions of samples where he had said 4 this looks like, for example, single 5 positive dilution, this looks unusual, 6 please have -- or have the counter 7 verify the count for accuracy. 8 BY MR. SCHNELL: 9 Q. And were there other criteria 10 that you recall him pointing out to you which 11 led him to direct you to have the counter do a 12 recheck? 13 A. I don't recall. The one I 14 recall is a single positive dilution. I don't 15 recall others. 16 Q. And when you say a single -- a 17 neutralization at a single positive dilution, 18 what does that mean? 19 A. It means that there are eight 20 dilutions of -- or actually rephrase it. 21 Neutralization at a single dilution. It means 22 that there are eight dilutions of a serum 23 tested. In the anti-IgG assay there is 24 something called a prozone effect, meaning 25 that the neutralization -- as the serum</p>	<p style="text-align: right;">Page 444</p> <p>1 directly -- the plaque visibility or clarity 2 is not directly related to the anti-IgG. 3 Q. And when you found a positive 4 neutralization of the single dilution, was it 5 always the case that it was an unreliable 6 result? 7 A. No. 8 Q. So sometimes they're reliable 9 and sometimes not? 10 A. Yes. 11 Q. Would you always retest those? 12 A. No. 13 Q. You would recount those? 14 A. We would check the plaques to 15 verify accuracy if there was a correction, if 16 the count was not accurate, in recounting it, 17 it turned out to not be neutralizing, that 18 result would be reported. 19 Q. Would you do a third time to 20 make sure that the second one was the accurate 21 one and not the first one? 22 A. I'm sorry, for the counting or 23 testing? 24 Q. For the counting. 25 A. Not that I recall.</p>
<p style="text-align: right;">Page 443</p> <p>1 dilutes out, there may not be neutralization 2 at the early dilutions, but then the prozone 3 means that there's a region of antibody 4 concentration where the anti-IgG is not 5 effective in enhancing neutralization. So 6 instead of having a neutralization curve where 7 you'd have neutralization that's diluting out, 8 you can have a sample where there's no 9 neutralization and at one or several dilutions 10 neutralization is detected. What single 11 dilution neutralization means that only one of 12 the eight dilutions is showing neutralization. 13 Q. And why would that be a result 14 that would lead you to believe that there was 15 a potential issue with accuracy? 16 A. At least one of the thoughts for 17 that was that the -- there may be something 18 about the staining or plaque visibility in 19 those wells that allowed for an inaccurate 20 count that then led to a reduced number of 21 plaques being counted. 22 Q. Didn't you testify that it had 23 to do with the anti-IgG? 24 A. The anti-IgG has an effect on 25 the prozone. The plaque count itself is not</p>	<p style="text-align: right;">Page 445</p> <p>1 Q. Well, then, how could you be 2 sure that the second one was more accurate 3 than the first one? 4 A. In the recheck, the counts were 5 only -- changes to the counts were only made 6 if there was confidence that the plaques were 7 miscounted in the first time. 8 Q. Why would there be more 9 confidence that the second count was more 10 accurate than the first count? 11 A. The confidence was that one was 12 looking more -- it's my interpretation that 13 someone was looking more carefully at the well 14 to make sure that something wasn't being 15 missed or miscounted. 16 Q. So it's your opinion that your 17 staff, when they did a recount, did it more 18 accurately the second time than the first 19 time? 20 A. Not -- I wouldn't say that as a 21 global statement, meaning that, for example, 22 in some rechecks the plaque counts there were 23 inaccuracies noted in some wells but not 24 globally across the assay. So if someone 25 counted the second time, it did not mean that</p>

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1 they saw differences but they were specific
 2 dilutions of samples that were more typically
 3 showing inaccurate counts.
 4 Q. You didn't institute any kind of
 5 two out of three rule with recounts?
 6 A. Not that I recall, no.
 7 Q. Wouldn't that have been more
 8 accurate than just recounting a second --
 9 recounting once and picking automatically the
 10 second count?
 11 A. I don't have a view on that.
 12 Q. You don't have a view that if
 13 you had a first count that you had a question
 14 about and you did a second count, that relying
 15 on the second count is more accurate, would be
 16 just as reliable as doing a third count and
 17 taking whichever was two out of three?
 18 MR. SANGIAMO: Object to the
 19 form. Asked and answered.
 20 THE WITNESS: Not necessarily.
 21 In fact, part of the recheck,
 22 recount -- I can't say with certainty
 23 that it was applied in every assay but
 24 the intention was to have the original
 25 counter recheck the counts and verify

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1 whether they agreed that there were
 2 miscounts or miscounted counts.
 3 BY MR. SCHNELL:
 4 Q. So when you had a question about
 5 the accuracy of a count, you would go back to
 6 the same counter?
 7 A. I can't say that that happened
 8 in -- well, I can't say it didn't happen in
 9 all cases, but that was in some of the assays
 10 my intention.
 11 Q. And it was your intention that
 12 having the same counter recount the original
 13 count would be more accurate than having a
 14 different counter come in?
 15 A. That in -- my interpretation at
 16 the time was that rather than add on the
 17 additional potential variability between
 18 counters, even though we had qualified all the
 19 counters, that it would be more reliable to
 20 have the original counter count. But in
 21 subsequent assays that wasn't always
 22 practical, meaning that those people might not
 23 be available to recheck plaque counts.
 24 Q. When you went back to the
 25 original counter and told them to recount, you

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1 would tell them to recount the entire assay?
 2 A. As best I can recall, I would
 3 identify that there was a question, identified
 4 for particular sample or plate and could they
 5 recheck that plate. I don't recall
 6 necessarily saying -- I don't recall saying to
 7 recheck the full assay.
 8 Q. So you would tell them to
 9 recheck the individual plate with which you
 10 had a question. Correct?
 11 A. I asked them to recheck the
 12 individual plate. I don't recall if I asked
 13 them to look at additional plates, but I don't
 14 recall them -- asking them to recall the full
 15 one -- to recheck the full assay.
 16 Q. When you asked them to recheck
 17 the plates because of a concern you had on
 18 accuracy, did you tell them what your concern
 19 was?
 20 A. As best I can recall, at least
 21 one example said there's a question about
 22 this. Well, in looking at it, at least one
 23 example, I said I see plaques that are missed,
 24 can you please verify whether or not you did
 25 it -- when you check it, that you get -- you

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1 see something. I don't think -- didn't give
 2 them a number to say, but just said I see a
 3 difference in counts than what you recorded,
 4 can you please recheck.
 5 Q. So you would actually do the
 6 recount first and then you would send it back
 7 to the counter for them to do the recount?
 8 MR. SANGIAMO: Object to the
 9 form.
 10 THE WITNESS: As best I can
 11 recall, the example I'm thinking of, I
 12 would look at -- the most
 13 straightforward one to me is looking at
 14 a plate, spots were put on the plate to
 15 identify where a plaque was counted. I
 16 would look at the plate and say I see
 17 spots that aren't marked by a Sharpie.
 18 So those look like plaques that were
 19 missed. Or I see spots next to
 20 something that doesn't look like a
 21 plaque. That would tell me that it
 22 looks like they're -- they counted
 23 something that wasn't a plaque.
 24 BY MR. SCHNELL:
 25 Q. So you wouldn't go back to the

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<p style="text-align: right;">Page 450</p> <p>1 counter and say, hey, we have a question about 2 this one, recount it, you would say, hey, we 3 have a question about this one because of X, Y 4 and Z, recount it to make sure you're 5 accurate? 6 MR. SANGIAMO: Object to the 7 form. 8 THE WITNESS: As best I can 9 recall, I would say that I -- can you 10 verify the counts for this. In some 11 cases saying I looked at the plate, I 12 see a different plaque, I see more 13 plaques or less plaques than what you 14 have got, can you please recheck. It 15 doesn't mean that I counted the plate 16 but I -- just looking at the plate, I 17 can see that something was either not 18 being counted or counted as a plaque 19 that didn't look like a plaque. 20 BY MR. SCHNELL: 21 Q. Now, this positive neutralization 22 of a single dilution occurs predominantly in 23 pre-vaccination samples because of the prozone 24 effect. Correct? 25 A. I don't know that that's</p>	<p style="text-align: right;">Page 452</p> <p>1 sense that it happened on the pre-vaccination 2 side? 3 A. No. 4 Q. Doesn't the prozone effect mask 5 neutralization? 6 A. No. 7 Q. It doesn't? 8 A. It doesn't mask neutralization 9 that was going to happen in the absence of 10 anti-IgG. 11 Q. Is there a difference in terms 12 of neutralization depending on whether 13 anti-IgG is part of the solution? 14 A. There's -- if one titrates 15 serum, I don't believe there's a difference in 16 quality of the antibody that's being detected. 17 If you had -- part of the -- this is largely 18 not based strictly on Protocol 007 experience 19 but other neutralization experiments, for 20 example, Protocol 006 where we tested at 21 higher serum concentrations. For example, we 22 could have a serum that neutralizes at 1 to 2 23 or 1 to 4 -- I don't recall 1 to 2 is the 24 first exposure. For example, 1 to 4 dilution 25 or 1 to 8 dilution, that would neutralize</p>
<p style="text-align: right;">Page 451</p> <p>1 correct. I agree with the prozone effect but 2 I don't recall that it's specific or happens 3 more frequently in the pre-vaccination sera. 4 Q. In your experience with this 5 assay, that wasn't the case. In virtually 6 every instance when there was a positive 7 neutralization at a single dilution, it was a 8 pre-positive and not a post-positive? 9 MR. SANGIAMO: Object to the 10 form. Asked and answered. 11 THE WITNESS: As best I can 12 recall, there were -- I don't recall 13 the actual numbers but there were 14 single positive dilution samples in 15 post-vaccination sera as well as 16 pre-vaccination sera. 17 BY MR. SCHNELL: 18 Q. But I'm saying in terms of the 19 vast majority where this occurred, it occurred 20 on the pre-vaccination side. Isn't that 21 correct? 22 A. I do not know that that's 23 correct. 24 Q. Well, in terms of how the 25 prozone effect works, wouldn't it make more</p>	<p style="text-align: right;">Page 453</p> <p>1 whether you had anti-IgG or not at that 2 dilution. It's much more likely at a higher 3 dilution. In the anti-IgG assay, knowing that 4 there's a prozone effect and to conserve sera 5 volumes, we started a 1 to 32 dilution. So we 6 did not have the capability of seeing whether 7 or not serum would have been positive at 1 to 8 4, 1 to 8 or 1 to 16 dilution. So my 9 expectation is that the anti-IgG would not 10 mask neutralization if it was going to happen 11 at a higher serum concentration. But we did 12 not test those higher serum concentrations. 13 Q. The neutralization that you're 14 talking about when it comes to anti-IgG, are 15 you talking about just mumps neutralization? 16 MR. SANGIAMO: Object to the 17 form. 18 THE WITNESS: I'm talking about 19 mumps plaque reduction. 20 BY MR. SCHNELL: 21 Q. Anti-IgG also leads to 22 neutralization of non-mumps antibodies. 23 Correct? 24 MR. SANGIAMO: Object to the 25 form. And asked and answered actually.</p>

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<p style="text-align: right;">Page 454</p> <p>1 THE WITNESS: The anti-IgG is 2 not specific for mumps antibodies so 3 it's capable of binding to other 4 antibodies. Whether or not it 5 neutralizes or not, I don't -- I can't 6 say. 7 BY MR. SCHNELL: 8 Q. So how do you know, then, if 9 you're using anti-IgG, whether the 10 neutralization that occurs is mumps 11 neutralizing or non-mumps neutralizing? 12 A. That was addressed in the -- the 13 specificity was an aspect that was addressed 14 as part of the validation plan to demonstrate 15 mumps specificity. 16 MR. SCHNELL: Can you, please, 17 repeat the question? 18 - - - 19 (The court reporter read the 20 pertinent part of the record.) 21 - - - 22 THE WITNESS: So anti-IgG on its 23 own does not neutralize mumps. We 24 showed in a paper by Sato from the FDA 25 for a similar effect. In our studies</p>	<p style="text-align: right;">Page 456</p> <p>1 specificity studies that were part of the 2 validation, we took sera, absorbed it with 3 measles, mumps, rubella antigen, given these 4 were MMR recipients and we're comparing pre- 5 and post-vaccination sera. The boost in titer 6 would indicate -- between pre- and 7 post-vaccination sera would indicate that 8 within that time frame between the two bleeds 9 there was a boost in the antibody. And then 10 with the absorption of measles, mumps, rubella 11 antigen demonstrated mumps, that absorbed with 12 mumps antigen reduced the neutralization 13 capacity of the serum more than the other 14 antigens, suggesting that the antibodies were 15 being attacked that were mumps specific. 16 Q. I think it was 50 percent 17 specificity. Correct? 18 A. That's not my interpretation of 19 the results. 20 Q. What was your interpretation? 21 A. My interpretation of the results 22 was that the antibody titers were reduced more 23 significantly by mumps than any of the 24 other -- than measles or rubella. And some of 25 the sera, some of the sera were, from my view,</p>
<p style="text-align: right;">Page 455</p> <p>1 we did -- did studies absorbing sera 2 with measles, mumps, rubella antigens 3 to demonstrate mumps specificity of the 4 neutralization. 5 BY MR. SCHNELL: 6 Q. So if you mixed anti-IgG with 7 human serum, it's going to neutralize -- it's 8 going to show neutralization of mumps 9 neutralizing antibodies and it's also going to 10 show a neutralization of non-mumps antibodies. 11 Correct? 12 MR. SANGIAMO: Object to the 13 form. 14 THE WITNESS: It could -- in 15 this assay we have -- there's -- the 16 indicator virus is mumps in the assay. 17 So we're detecting mumps specific 18 neutralization. 19 BY MR. SCHNELL: 20 Q. But how? If there is anti-IgG 21 in there, how do you know if it's the 22 antibodies that are mumps neutralizing or the 23 other types of antibodies that the anti-IgG 24 combined with? 25 A. In an example I gave, the</p>	<p style="text-align: right;">Page 457</p> <p>1 not a valuable, meaning they were negative for 2 all the absorbing antigens. 3 For the pediatric sera, as best 4 I recall, two -- I don't know pediatric or 5 adult sera, two of the four showed less or 6 some effect of rubella absorption on titers, 7 but I would argue that those, the lack of 8 absorbing -- more efficiently absorbing out 9 mumps antibodies for those who are -- 10 absorbing out the antibodies for mumps from 11 those sera may be a reflection of the titer of 12 those sera rather than the specificity itself, 13 meaning that we're adding a fixed amount of 14 antigen to absorb the antibodies. We don't 15 have a guarantee that we're adding enough 16 antigen to absorb out all of the antibodies. 17 Q. So the test that you say you 18 conducted, measles, mumps, and rubella, didn't 19 show that 100 percent of the neutralizing 20 antibodies were mumps neutralizing. Right? 21 MR. SANGIAMO: Object to the 22 form. 23 THE WITNESS: No, in fact, there 24 are published absorption experiments. 25 I've never seen one that showed 100</p>

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<p style="text-align: right;">Page 458</p> <p>1 percent reduction of antibody 2 specificity with the absorption. 3 BY MR. SCHNELL: 4 Q. So some of the neutralization 5 that occurs when you're using anti-IgG in the 6 mumps testing that you did would have resulted 7 from non-mumps neutralizing antibodies. 8 Correct? 9 MR. SANGIAMO: Object to the 10 form. 11 THE WITNESS: From my 12 interpretation, that's not a conclusion 13 that I would make from that -- from the 14 specificity data. 15 BY MR. SCHNELL: 16 Q. So is your testimony that 100 17 percent of the neutralization that occurred in 18 the AIGENT testing was mumps neutralizing 19 antibodies? 20 A. My testimony is that the 21 specificity study demonstrated that the assay 22 was showing specificity for mumps. I can't 23 speak to whether it's 100 percent. I don't 24 have familiarity or insight into the 25 application to say whether one can say it's</p>	<p style="text-align: right;">Page 460</p> <p>1 antibodies? 2 A. Only IgG antibodies. 3 Q. Okay. So is mumps the only one? 4 A. There are other potential IgG 5 antibodies. 6 Q. Flu? Could it bind with flu 7 antibodies? 8 A. I can't exclude it. I don't 9 know what sera -- what the recipients of the 10 vaccine, what antibodies they would likely 11 have. But I would agree in theory, if it's an 12 appropriate IgG antibody, it could bind to the 13 anti-IgG. 14 Q. So what are some other IgG 15 antibodies that it could potentially bind to? 16 A. Any -- whatever IgGs are in 17 serum. 18 Q. What are those? 19 A. In an infant I don't know what -- 20 Q. Do you know any? 21 A. I don't -- I just would be 22 pulling virus names out of the air. 23 Q. It could be measles. Right? 24 A. Yes. 25 Q. It could be rubella?</p>
<p style="text-align: right;">Page 459</p> <p>1 100 percent. All I can say is that the assay 2 from my view demonstrated specificity -- 3 absorption experiments demonstrated 4 specificity. Whether one can assign 100 5 percent, that's -- it's not a term that I'm 6 familiar with or have any familiarity with to 7 say whether the 100 percent value applies. 8 Q. So you just don't recall one way 9 or the other? 10 MR. SANGIAMO: Object to the 11 form. 12 THE WITNESS: I would say my 13 recollection is that the absorption 14 experiment showed mumps specificity. 15 How one then assigns what -- not saying 16 it's specific or nonspecific, I'm not 17 familiar with how one assigns a percent 18 value. 19 BY MR. SCHNELL: 20 Q. You can see that anti-IgG binds 21 with any kind of antibody in the blood. 22 Right? 23 A. No. 24 Q. So it binds with mumps 25 antibodies, right, mumps neutralizing</p>	<p style="text-align: right;">Page 461</p> <p>1 A. Yes. 2 Q. It could be flu? 3 MR. SANGIAMO: Object to the 4 form. 5 THE WITNESS: I don't know. The 6 measles, mumps, rubella I agree to 7 because they're given more vaccine. As 8 far as flu, I don't know. Again, I 9 would agree in theory a flu antibody 10 could bind. Whether or not the infants 11 would have flu anti-IgG, I don't know. 12 BY MR. SCHNELL: 13 Q. So what steps, if any, did you 14 take to control for the possibility that the 15 anti-IgG was showing a false neutralization 16 because it was detecting or it was allowing 17 you to detect in the AIGENT testing non-mumps 18 neutralizing antibodies? 19 MR. SANGIAMO: Objection. Asked 20 and answered. 21 THE WITNESS: The absorption 22 experiments from my view demonstrated 23 the mumps specificity. Another aspect 24 which is my -- I've seen it in other 25 publications, I don't -- I can't recall</p>

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1 with certainty if this was included in
 2 the discussion of the current assay, is
 3 that we have a pre-vaccination serum
 4 and then a post-vaccination serum. If
 5 they're given MMR, you only -- the
 6 expectation would be that the infants
 7 are only going to make antibodies to
 8 those three viruses in that time
 9 period. So if one had a question about
 10 flu antibodies or other antibodies, it
 11 would be unlikely that those --
 12 comparing the pre- and post-vaccination
 13 titers, that they would change
 14 concomitant with the MMR vaccination or
 15 integral between bleeds with the MMR
 16 vaccination.
 17 BY MR. SCHNELL:
 18 Q. Were the subjects in the AIGENT
 19 testing screened beforehand to make sure that
 20 they didn't -- their blood didn't contain any
 21 other IgG?
 22 A. I'm not aware of any screening.
 23 MR. SANGIAMO: Gordon, we've
 24 been going about an hour and five
 25 minutes. If you get to a good stopping

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1 point.
 2 MR. SCHNELL: A few minutes.
 3 BY MR. SCHNELL:
 4 Q. So the AIGENT testing had
 5 controls. Right?
 6 A. The AIGENT assay had a control
 7 of those serum, meaning virus anti-IgG in the
 8 absence of serum. It had a, call it a
 9 control, but a mock sample which is the
 10 control -- sorry, that's not right. The
 11 control which is the virus anti-IgG and no
 12 serum. Virus anti-IgG and no serum. And then
 13 there were adult -- two control sera in each
 14 assay. And then uninoculated controls.
 15 Q. For the negative control you
 16 used the mock control I believe you said?
 17 A. That's not a negative -- I guess
 18 one could call it a negative control. I don't
 19 view it as a negative control. I view that as
 20 the baseline.
 21 Q. So how did that control, if at
 22 all, control for the possibility that anti-IgG
 23 was going to lead to false neutralization?
 24 A. That sample included anti-IgG in
 25 the absence of serum. So it would -- that was

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1 a control to verify that the anti-IgG was
 2 not -- would account for -- would verify the
 3 anti-IgG was not neutralizing mumps.
 4 Q. How could it do that if the
 5 control didn't have serum?
 6 A. That's the -- the intent of that
 7 control was to demonstrate -- or in previous
 8 experiments we looked at adding anti-IgG or
 9 not to virus, and there was no impact and
 10 confirming the results of the Sato paper. So
 11 it's a control not for serum but for the
 12 anti-IgG. We did not have a control for --
 13 for example, we did not have a negative serum
 14 control.
 15 Q. Did the Sato paper talk about
 16 controlling for anti-IgG?
 17 A. I'm sorry, in what way?
 18 Q. In any way.
 19 A. I recall that they -- the
 20 publication described dilutions of anti-IgG.
 21 As best I can recall, they had a -- no serum
 22 control. I don't recall if they had other --
 23 what other controls, if any, were described.
 24 Q. Again, if there's a risk that
 25 using anti-IgG will bind with non-mumps

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1 neutralizing antibodies, how can you control
 2 for that possibility if you don't use serum in
 3 the control?
 4 A. As we state here, in the case of
 5 a paired sera, the pre-vaccination serum is
 6 not intended as a control but it serves as
 7 a -- in effect a control, meaning that if
 8 pre-vaccination serum are predominantly
 9 negative, post-vaccination serum are
 10 seroconverting, that that pre-vaccination
 11 serum indicates that -- negative
 12 pre-vaccination serum result indicates that
 13 there's no detectable mumps antibody or
 14 other -- it is my interpretation no mumps
 15 antibody from your description would -- if
 16 there's any potential -- would address the
 17 absence of mumps specific antibody in those
 18 sera. Whether or not other antibodies that
 19 were in there could or would or could
 20 neutralized mumps, we don't have other viruses
 21 in there to see what other viruses might be
 22 present and neutralized.
 23 Q. So how could you be sure, maybe
 24 this wasn't important to your experiment, but
 25 I would assume it would be, how could you be

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1 sure that the neutralization results you were
 2 getting in the AIGENT testing was specific,
 3 100 percent specific to not -- to mumps
 4 neutralizing antibodies?
 5 MR. SANGIAMO: Object to the
 6 form.
 7 THE WITNESS: Again, going back
 8 to the validation study, as best I
 9 recall, those -- the results of the
 10 validation study were presented both to
 11 Merck and to CBER. They did not raise
 12 concerns over that specificity. My
 13 conclusion from that was that the assay
 14 was specific, demonstrated to be
 15 specific for mumps.
 16 BY MR. SCHNELL:
 17 Q. If you had used a non-immune
 18 serum, a non-immune control, meaning
 19 non-immune serum in the control, and anti-IgG,
 20 wouldn't that have told you exactly whether or
 21 not there was neutralizing antibodies caused
 22 by the anti-IgG that were not mumps
 23 neutralizing antibodies?
 24 MR. SANGIAMO: Object to the
 25 form.

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1 THE WITNESS: No. That has one
 2 major caveat to my understanding in
 3 that negative serum is, from my
 4 understanding, not an absolute value,
 5 meaning it depends on the assay that's
 6 used to show that it's devoid of
 7 antibodies to mumps.
 8 BY MR. SCHNELL:
 9 Q. Didn't you use it for the ELISA
 10 testing?
 11 MR. SANGIAMO: Object to the
 12 form.
 13 BY MR. SCHNELL:
 14 Q. Wasn't that critical to the
 15 ELISA testing?
 16 MR. SANGIAMO: Object to the
 17 form.
 18 THE WITNESS: I'm not familiar
 19 with the ELISA -- it's a different
 20 assay, so I don't --
 21 BY MR. SCHNELL:
 22 Q. You don't know what controls, if
 23 any, they used?
 24 MR. SANGIAMO: Object to the
 25 form.

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1 THE WITNESS: I'm not -- yeah, I
 2 don't know the specific controls that
 3 they used.
 4 MR. SCHNELL: Okay. We can take
 5 a break.
 6 VIDEOGRAPHER: The time is now
 7 10:16. This ends disc one.
 8 - - -
 9 (A recess was taken.)
 10 - - -
 11 VIDEOGRAPHER: The time is now
 12 10:33. This begins disc two. You may
 13 proceed.
 14 BY MR. SCHNELL:
 15 Q. Dr. Krah, in terms of the
 16 interim analysis, taking us back to the flow
 17 of the plaque counting process, in terms of
 18 the interim analysis, when you were reviewing
 19 the spreadsheet which had the data that
 20 derived from the plaque counting, and you were
 21 looking for criteria to confirm accuracy, was
 22 that something that you were directed to do?
 23 A. I would say the single positive
 24 dilution aspect, as best I recall, was
 25 something in reviewing the data with Emilio

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1 Emilio that he, I wouldn't say directed, but
 2 pointed out that those were ones that he
 3 thought were worthy of verifying plaque
 4 counts. So I wouldn't call it a directive,
 5 but in doing that and realizing that some of
 6 the counts were not accurate became something
 7 that seemed appropriate to continue, from my
 8 interpretation to continue doing. So one
 9 point it is a directive but something that
 10 came out of initial discussions with Emilio.
 11 Q. When you say that in reviewing
 12 this and you finding out that the plaque
 13 counts weren't accurate in this regard, how
 14 did you confirm that they weren't accurate?
 15 A. Well, not -- the original
 16 counters were, as I indicated, I can't -- I
 17 don't recall in each case the original counter
 18 was the one that verified it, but I had
 19 confidence that the person doing the recheck
 20 was taking an accurate count. I would point
 21 out that not all of them -- some were accurate
 22 and some weren't. So it wasn't always -- in
 23 each case where there was a check, it did not
 24 result in a correction.
 25 Q. But you always believed that the

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<p style="text-align: right;">Page 470</p> <p>1 second count was more accurate than the first 2 count. Correct? 3 A. That's my best recollection, 4 yes. 5 Q. What's that based on? 6 A. My confidence -- it's based on 7 my confidence in the first count plaques were 8 miscounted, the person realized that in the 9 recount and then had a -- in some cases, not 10 all the cases resulted in a change, but that 11 their recount verified whether the original 12 result was accurate or the correction was 13 accurate and that recount, the recheck gave me 14 confidence that the person verified the 15 accurate plaque count. 16 Q. So these were criteria for 17 checking views to determine whether or not 18 there should be recounts. Correct? That's 19 what we've been talking about, this criteria 20 for the interim analysis was the criteria that 21 you were guided by in determining whether or 22 not there should be recounts? 23 MR. SANGIAMO: Object to the 24 form. 25 THE WITNESS: I'm not sure I</p>	<p style="text-align: right;">Page 472</p> <p>1 post-vaccination serum that made that sample 2 result invalid, the pair would be retested. 3 We always tested the sera as a pair in the 4 same assay. Which the point there being that 5 if, for example, one of the serum -- like a 6 pre-vaccination serum result was valid, a 7 post-vaccination serum was not valid, we would 8 retest the pair together. To get a valid 9 result, you needed a valid pre- and 10 post-vaccination serum result. 11 Q. So what were the circumstances 12 that would lead to a pre- or post-vaccination 13 sample being invalid? 14 A. In the first third, I don't 15 recall the specific example. The second third 16 and third third, for example, there were, I 17 believe, what was described in the workbook as 18 an invalid dilution, meaning a -- for example, 19 if for a given serum dilution we have 20 triplicate wells, the samples are inoculated 21 in triplicate wells, we need at least two -- 22 values for two of those wells to have a valid 23 result for that well; meaning that if we only 24 had one result out of the three replicates, 25 that would be an invalid dilution. So there</p>
<p style="text-align: right;">Page 471</p> <p>1 understand the question. 2 BY MR. SCHNELL: 3 Q. So the four criteria you 4 outlined, positive neutralization single 5 dilution, erratic neutralization, plaques and 6 unaffected cell control and pre-positives to 7 post-negatives, those were criteria that you 8 identified before that you looked at to 9 determine whether or not you were going to 10 direct a recount? 11 A. Those were conditions in which 12 we looked at the plates and did a recount to 13 verify the accuracy of the counts. 14 Q. So what about for retesting, was 15 there also a set of criteria that you were 16 governing -- that you were looking towards to 17 determine whether or not a retest was 18 appropriate? 19 A. There was a criteria for -- 20 there was a criteria for retest that involved 21 an invalid result for -- in the first part I 22 don't recall if this applies. The point I was 23 trying to -- I was thinking I was trying to 24 make is that in one of the -- if there was an 25 aspect to our pre-vaccination serum or a</p>	<p style="text-align: right;">Page 473</p> <p>1 would be no opportunity to determine whether 2 that serum was neutralizing or not. 3 Q. Any other examples? 4 A. No. We had cases where, besides 5 the extra -- there was extra -- extra 6 variability criteria was part of that. And in 7 some assays we're having, for want of a better 8 description, tearing of the monolayers, they 9 need some healing of the cells that prevented 10 getting an accurate count for those wells. 11 Those would then result in, from my 12 interpretation, a similar invalid dilution. 13 There may be other cases. Those are two that 14 comes to mind. 15 Q. So with the extra variability 16 criteria, what would that entail? 17 A. That -- as best I understand it, 18 it was a value established by our 19 statistician. It's not an area I'm fluent in. 20 My general understanding is that it looked at 21 the variability between the triplicate well 22 values or having duplicate wells would still 23 be valid. So looking at variability between 24 the duplicate and triplicate wells. And then 25 there was a calculation involved to, as best I</p>

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<p style="text-align: right;">Page 474</p> <p>1 recall, identify a range that is statistically 2 acceptable between, as best I recall, the high 3 and the low value in that range. So my 4 understanding it's basically looking to see if 5 the numbers, if the replicate values are 6 unusually unlike each other. 7 Q. Was positive neutralization in a 8 single dilution ever used as a criteria for 9 retesting? 10 A. Positivity of a single dilution 11 was used, not specifically for pre-positive. 12 Q. So that was also used as a 13 criteria for retesting? 14 A. As best I can recall, a single 15 positive dilution was flagged for not 16 necessarily -- I'm sorry, not for retesting. 17 For plaque count as a first check, not -- 18 there are some samples that were tested, 19 retested as part of an understanding the assay 20 and monitoring the assay. There were single 21 positive dilutions. But in those cases, the 22 result of the original test was always 23 reported if the original result was valid. 24 Q. So getting back to the interim 25 analysis, I want to make sure I understand the</p>	<p style="text-align: right;">Page 476</p> <p>1 number, the count number for that well yet. 2 Q. So you recall instances at least 3 where you were counting where you would do a 4 count, and you'd mark it on the plate and then 5 you would check your count and get a different 6 number? 7 A. It's not a -- I wouldn't 8 characterize it as a check. As part of the 9 routine counting, after I put spots in the 10 plate, I tilt the plate back and forth to make 11 sure that I wasn't missing something. So it's 12 not a recount or a check but a verification 13 that something wasn't being missed. 14 Q. So you didn't double check your 15 work, you would just count once, give it a 16 little look and that's that. Right? 17 MR. SANGIAMO: Object to the 18 form. And asked and answered. 19 THE WITNESS: As best -- as far 20 as -- I don't recall doing -- unless it 21 was part of a recheck of additional 22 assay plates later, I would not recheck 23 or recount that particular plate. 24 BY MR. SCHNELL: 25 Q. And you didn't direct your staff</p>
<p style="text-align: right;">Page 475</p> <p>1 path. So the counter would first look at the 2 plate, count the plaques, and each time they 3 counted the plaque, they would mark somewhere 4 on the plate a dot for each plaque they 5 counted. Correct? 6 A. That's my understanding and 7 recollection of the -- how they were counted. 8 Q. Then the plaque count, would 9 they double check that? 10 A. Not that I'm aware of. From my 11 own personal experience, as part of the 12 counting of the plate, I would mark the spots 13 and then give a second look, not recheck, but 14 look to see that I didn't miss something. 15 Q. And were there instances where 16 you missed something? 17 A. I recall cases where the 18 plates -- occasionally the plaques aren't 19 visible. It may be like -- hard to describe, 20 but they could be at the corner of the well so 21 you need to tilt the plate back and forth a 22 bit to make sure that you're seeing all the 23 surface of the wells. But I considered that 24 not a recheck but part of the original 25 counting. Because I hadn't finalized the</p>	<p style="text-align: right;">Page 477</p> <p>1 to either? 2 A. No. 3 Q. Would that have made the 4 counting more accurate? 5 A. From a statistical criteria, I 6 can't say whether it would have. My 7 understanding was that when we're doing the 8 plaque count qualification, it's typically a 9 person counts the plate, set of plates, 10 another person counts the set of plates. We 11 were doing the plaque count comparison with a 12 single round of counting. So whether or not a 13 second round of counting would have had an 14 impact, I don't have a thought. 15 Q. Do you recall during the 16 counting process that you would on occasion go 17 to some of your counters while they were 18 counting and help them count? 19 A. I recall some counters when they 20 were counting saying I'm having trouble seeing 21 these plaques, they look kind of faint or 22 they're not readily visible, can you take a 23 look at this and verify that I'm counting 24 accurately. 25 Q. Do you recall finding that there</p>